Scientific Information Center

SEARCH REQUEST FORM 263494

RECEIVED JUN 10 2008 STIC

Requester's Full Name: Cecilia Jaiek Examiner #: 82613 Date: 6/3/08
Art Unit: 1624 Phone Number: 2-4931 Serial Number: 10516971
Location (Bldg/Room): REMSEN (Mailbox #): 5C18 Results Format Preferred (circle): PAPER DISK

To ensure an efficient and quality search, please attach a copy of the cover sheet, claims, and abstract or fill out the following:

Title of Invention: See Bib Data Sheet 1/9

Inventors (please provide full names):

Earliest Priority Date:

Search Topic:
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known.

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

See claims attached. Please do structure search and inventor name (s) search. Display results to show identification of source, and R.N #, compound name & structure of identified compounds. Search compounds of Formula I.

RECEIVED JUN 13 2008 STIC

Please call with any questions

STAFF USE ONLY

Searcher: _____
Searcher Phone #: _____
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Date Searcher Picked Up: _____
Date Completed: _____
Searcher Prep & Review Time: _____
Online Time: _____

Type of Search
_____ NA Sequence (#)
_____ AA Sequence (#)
_____ Structure (#)
_____ Bibliographic
_____ Litigation
_____ Fulltext
_____ Other

Vendors and cost where applicable
_____ STN _____ Dialog
_____ QuestelOrbit _____ LexisNexis
_____ Westlaw _____ WWW/Internet
_____ In-house sequence systems
_____ Commercial _____ Oligomer _____ Source/Length
_____ Interference _____ SPDI _____ Encode/Translate
_____ Other (specify)

=> fil hcaplus

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FILE LAST UPDATED: 17 Jun 2008 (20080617/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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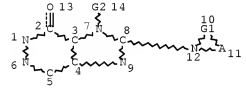
L1 STR



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GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE
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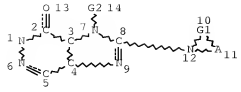

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STEREO ATTRIBUTES: NONE
L5          344 SEA FILE=REGISTRY SUB=L3 SSS FUL L4
L6           15 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5


=>
=> d ibib abs hitstr 16 1-15

L6   ANSWER 1 OF 15  HCAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2008:234007  HCAPLUS  Full-text
DOCUMENT NUMBER:          148:449563
TITLE:                    Synthesis of 2-bromo-7-methyl-3,5-dihydro-imidazo[4,5-
                          d]pyridazin-4-one and 3-alkyl-2-bromo-3,5-dihydro-
                          imidazo[4,5-d]pyridazin-4-one and their selective
                          elaboration
AUTHOR(S):                Eckhardt, Matthias; Hauel, Norbert; Langkopf, Elke;
                          Himmelsbach, Frank
CORPORATE SOURCE:         Department of Chemical Research, Boehringer Ingelheim
                          Pharma GmbH & Co. KG, Biberach, 88400, Germany
SOURCE:                   Tetrahedron Letters (2008), 49(12), 1931-1934
                          CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER:                Elsevier Ltd.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB    Two synthetic routes to the versatile title 3,5-dihydroimidazo[4,5-
      d]pyridazin-4-ones were developed that allow the production of multigram
      quantities without the need of any chromatog. purification  Broad and
      selective elaboration of the heteroarom. scaffolds was also accomplished.
IT    813462-72-5P 813462-73-6P
      RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
      (Reactant or reagent)
         (preparation of dihydroimidazopyridazinones)
RN    813462-72-5  HCAPLUS
CN    Carbamic acid, N-[1-[1-(2-butyn-1-yl)-6,7-dihydro-7-oxo-1H-imidazo[4,5-
      d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester  (CA INDEX
      NAME)
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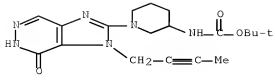
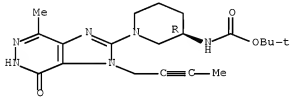


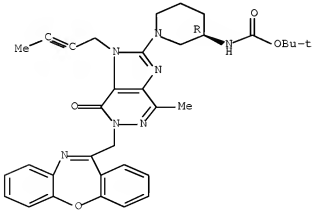
RN 813462-73-6 HCAPLUS
CN Carbamic acid, N-[(3R)-1-[1-(2-butyn-1-yl)-6,7-dihydro-4-methyl-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)

Absolute stereochemistry.



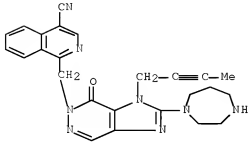
IT 813462-67-8P 855789-80-9P 855789-81-0P
1018950-86-1P 1018950-93-0P 1018951-03-5P
1018951-09-1P 1018951-21-7P 1018951-23-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of dihydroimidazopyridazinones)
RN 813462-67-8 HCAPLUS
CN Carbamic acid, N-[(3R)-1-[1-(2-butyn-1-yl)-6-(dibenz[b,f][1,4]oxazepin-11-ylmethyl)-6,7-dihydro-4-methyl-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)

Absolute stereochemistry.

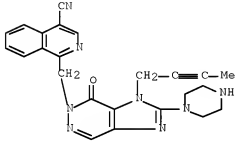


RN 855789-80-9 HCAPLUS
CN 4-Isoquinolinecarbonitrile, 1-[[3-(2-butyn-1-yl)-2-(hexahydro-1H-1,4-

diazepin-1-yl)-3,4-dihydro-4-oxo-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-
(CA INDEX NAME)

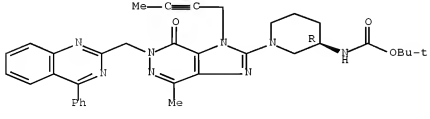


RN 855789-81-0 HCAPLUS
CN 4-Isoquinolinecarbonitrile, 1-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]- (CA INDEX NAME)

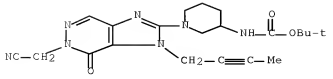


RN 1018950-86-1 HCAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.

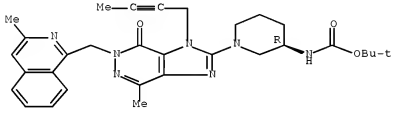


RN 1018950-93-0 HCAPLUS
CN INDEX NAME NOT YET ASSIGNED

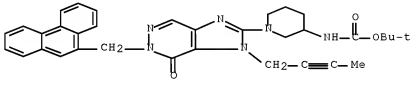


RN 1018951-03-5 HCAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



RN 1018951-09-1 HCAPLUS
CN INDEX NAME NOT YET ASSIGNED



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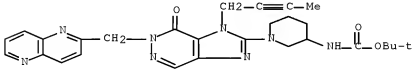
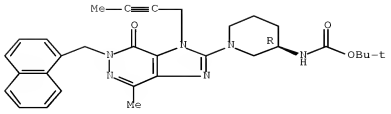
CN INDEX NAME NOT YET ASSIGNED



RN 1018951-23-9 HCAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:621842 HCAPLUS Full-text
DOCUMENT NUMBER: 147:203595
TITLE: Comparison of efficacies of a dipeptidyl peptidase IV inhibitor and α-glucosidase inhibitors in oral carbohydrate and meal tolerance tests and the effects of their combination in mice
AUTHOR(S): Yamazaki, Kazuto; Inoue, Takashi; Yasuda, Nobuyuki; Sato, Yoshiaki; Nagakura, Tadashi; Takenaka, Osamu; Clark, Richard; Saeki, Takao; Tanaka, Isao
CORPORATE SOURCE: Tsukuba Research Laboratories, Eisai Co., Ltd., 5-1-3, Tokodai, Tsukuba, Ibaraki, 300-2635, Japan
SOURCE: Journal of Pharmacological Sciences (Tokyo, Japan) (2007), 104(1), 29-38
CODEN: JPSTGJ; ISSN: 1347-8613
PUBLISHER: Japanese Pharmacological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB E3024 (3-but-2-ynyl-5-methyl-2-piperazin-1-yl-3,5-dihydro-4H-imidazo[4,5-d]pyridazin-4-one tosylate) is a dipeptidyl peptidase IV (DPP-IV) inhibitor. Since the target of both DPP-IV inhibitors and α-glucosidase inhibitors is the lowering of postprandial hyperglycemia, we compared antihyperglycemic effects for E3024 and α-glucosidase inhibitors in various oral carbohydrate and meal tolerance tests using normal mice. In addition, we investigated the combination effects of E3024 and voglibose on blood glucose levels in a meal tolerance test using mice fed a high-fat diet. ER-235516-15 (the trifluoroacetate salt form of E3024, 1 mg/kg) lowered glucose excursions consistently, regardless of the kind of carbohydrate loaded. However, the efficacy of acarbose (10 mg/kg) and of voglibose (0.1 mg/kg) varied with the type of carbohydrate administered. The combination of E3024 (3 mg/kg) and voglibose (0.3 mg/kg) improved glucose tolerance additively, with the highest plasma active glucagon-like peptide-1 levels. This study shows that compared to α-glucosidase inhibitors, DPP-IV inhibitors may have more consistent efficacy to reduce postprandial hyperglycemia, independent of the types of carbohydrate contained in a meal, and that the combination of a DPP-IV inhibitor and an α-glucosidase inhibitor is expected to be a promising option for lowering postprandial hyperglycemia.

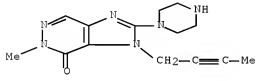
IT 635717-66-7, ER 235516-15 635722-43-9, E3024
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparison of efficacies of a dipeptidyl peptidase IV inhibitor and α-glucosidase inhibitors in oral carbohydrate and meal tolerance tests and the effects of their combination in mice)

RN 635717-66-7 HCAPLUS

CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-methyl-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635717-65-6
CMF C14 H18 N6 O



CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635722-43-9 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-methyl-2-(1-piperazinyl)-, 4-methylbenzenesulfonate (1:1) (CA INDEX NAME)

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CRN 635717-65-6
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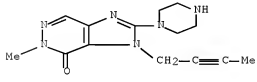

CM 2

CRN 104-15-4
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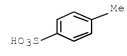

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:259319 HCAPLUS Full-text
DOCUMENT NUMBER: 146:281045
TITLE: Method for preparation of pharmaceutical composition having improved disintegradability
INVENTOR(S): Ueki, Yousuke
PATENT ASSIGNEE(S): Eisai R & D Management Co., Ltd., Japan
SOURCE: PCT Int. Appl., 58pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007026864	A1	20070308	WO 2006-JP317307	20060901
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RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006285673	A1	20070308	AU 2006-285673	20060901
CA 2620594	A1	20070308	CA 2006-2620594	20060901
KR 2008047546	A	20080529	KR 2008-705195	20080229
PRIORITY APPLN. INFO.:			JP 2005-253305 A	20050901
			WO 2006-JP317307 W	20060901

AB A pharmaceutical composition or method has been keenly demanded which enables the pharmacol. effect of a pharmaceutical preparation to be developed rapidly without the need of upsizing of the pharmaceutical preparation or without the deterioration in quality which may be caused by the interaction between a pharmacol. active ingredient and a disintegrating agent contained in the pharmaceutical preparation Particularly, it is strongly demanded in a pharmaceutical preparation comprising an analgesic agent, a quick-acting hypoglycemic agent or the like which is required to exert its pharmacol. effect rapidly after administration, a pharmaceutical preparation containing an pharmacol. active ingredient in a high content, a pharmaceutical preparation containing two or more kinds of pharmacol. active ingredients, and the like. The object is to improve the disintegradability of a pharmaceutical composition without the need of upsizing of the pharmaceutical preparation or without the deterioration in quality which may be caused by the interaction between a pharmacol. active ingredient and a disintegrating agent contained in

the pharmaceutical composition Thus, disclosed is a method for preparation of a pharmaceutical composition having a short disintegration time, comprising the step of adding at least one disintegrating agent and at least one water-soluble salt which shows a pH value ranging from 3 to 9 when prepared in the form of an aqueous 2.5% solution to a pharmaceutical composition comprising a pharmaceutically active ingredient. Also disclosed is a premix composition in which a disintegrating agent and a water-soluble inorg. salt which shows a pH value ranging from 3 to 9 when prepared in the form of an aqueous 2.5% solution are mixed previously. For example, a dipeptidylpeptidase IV inhibitor (3-But-2-ynyl-5-methyl-2-piperazin-1-yl-3,5-dihydro-4H-imidazo[4,5-d]pyridazin-4-one tosylate) 77.8, mannitol 8.92, corn starch 14.1, low-substituted hydroxypropyl cellulose (L-HPC LH21) 21.15, hydroxypropyl cellulose (HPC-L) 3.53 g, were mixed with water q.s., and granulated. The obtained granules 209.2 mg was mixed with crystalline cellulose 34.5, NaCl 1.2, magnesium stearate 2.4 mg, and tabletted.

IT 635722-43-9

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(method for preparation of pharmaceutical composition having improved disintegradability)

RN 635722-43-9 HCAPLUS

CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-methyl-2-(1-piperazinyl)-, 4-methylbenzenesulfonate (1:1) (CA INDEX NAME)

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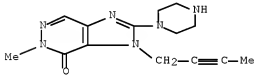
CRN 635717-65-6
CMF C14 H18 N6 O



CM 2

CRN 104-15-4
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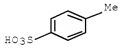

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:161801 HCAPLUS Full-text
DOCUMENT NUMBER: 146:372433
TITLE: Effects of the combination of a dipeptidyl peptidase

IV inhibitor and an insulin secretagogue on glucose and insulin levels in mice and rats

AUTHOR(S): Yamazaki, Kazuto; Yasuda, Nobuyuki; Inoue, Takashi; Yamamoto, Eiichi; Sugaya, Yukiko; Nagakura, Tadashi; Shinoda, Masanobu; Clark, Richard; Saeki, Takao; Tanaka, Isao

CORPORATE SOURCE: Tsukuba Research Laboratories, Eisai Co., Ltd., Ibaraki, Japan

SOURCE: Journal of Pharmacology and Experimental Therapeutics (2007), 320(2), 738-746
CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Several combination therapies have been tried for treating of type 2 diabetes to control more effectively fasting hyperglycemia and postprandial hyperglycemia. In this study, we have examined the effects of combining a novel, selective, and competitive dipeptidyl peptidase IV (DPP-IV) inhibitor, 3-but-2-ynyl-5-methyl-2-piperazin-1-yl-3,5-dihydro-4H- imidazo[4,5-d]pyridazin-4-one tosylate (E3024), with a representative of one of two types of insulin secretagogues, i.e., either glybenclamide (a sulfonylurea) or nateglinide (a rapid-onset/short-duration insulin secretagogue), on glucose and insulin levels in an oral glucose tolerance test (OGTT) using mice fed a high-fat diet. In addition, we have investigated the effects of these combinations on blood glucose levels in fasting rats. Two-way anal. of variance showed that the combination of E3024 and glybenclamide improved glucose tolerance additively and also caused a synergistic increase in insulin levels in the OGTT in mice fed a high-fat diet. In a similar way, the combination of E3024 and nateglinide ameliorated glucose tolerance additively and raised insulin levels additively. In fasting rats, coadministration of E3024 with glybenclamide or nateglinide treatment did not affect the glucose-lowering effects of the insulin secretagogues. Therefore, a DPP-IV inhibitor in combination with glybenclamide or nateglinide may be a promising option for the treatment of type 2 diabetes, and particularly, for controlling postprandial hyperglycemia in the clinic.

IT 635722-43-9, E 3024
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of combination of dipeptidyl peptidase IV inhibitor and insulin secretagogue on glucose and insulin levels)

RN 635722-43-9 HCAPLUS

CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-methyl-2-(1-piperazinyl)-, 4-methylbenzenesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 635717-65-6
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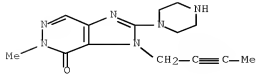
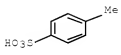


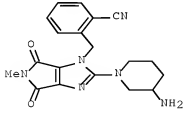
CM 2

CRN 104-15-4
CMF C7 H8 O3 S

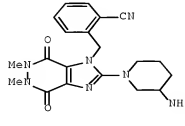


REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1190030 HCAPLUS Full-text
DOCUMENT NUMBER: 146:134585
TITLE: Xanthine mimetics as potent dipeptidyl peptidase IV inhibitors
AUTHOR(S): Kurukulasuriya, Ravi; Rohde, Jeffrey J.; Szczepankiewicz, Bruce G.; Basha, Fatima; Lai, Chunqui; Jae, Hwan-Soo; Winn, Martin; Stewart, Kent D.; Longenecker, Kenton L.; Lubben, Thomas W.; Ballaron, Stephen J.; Sham, Hing L.; von Geldern, Thomas W.
CORPORATE SOURCE: Metabolic Disease Research, Global Pharmaceutical Research and Development, Abbott Laboratories, Abbott Park, IL, 60064-6098, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(24), 6226-6230
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 146:134585
GI



I



II

AB Aminopiperidinyl-substituted fused imidazoles such as pyrroloimidazole I•HCl are prepared as xanthine mimetics using a copper-catalyzed cyclocondensation of bromoaryl guanidines as the key step; their inhibition of human dipeptidylpeptidase IV (DPPIV) and the selectivities of some of the compds.

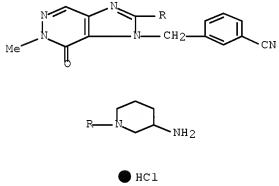
for DPPIV over DPP8, DPP9, and prolyl oligopeptidase are determined I binds to human DPPIV with a Ki value of 2 nM while binding to DDP8, DPP9, and prolyl oligopeptidase with Ki values > 3 μM. I is poorly bioavailable in rats, with a high clearance, low oral bioavailability, and low stability in the presence of rat plasma. Imidazolopyridazinedione II and an imidazoledicarboxamide related to I are prepared; II binds to DPPIV with a Ki value of 11 nM while binding to DDP8, DPP9, and prolyl oligopeptidase with Ki values > 3 μM and while being significantly more potent than I in the presence of plasma. I is not selective for human DPPIV over rat DPPIV. The crystal structure of I bound to human DPPIV is determined by X-ray crystallog.

IT 918931-39-2P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of aminopiperidinyl-substituted fused imidazoles as xanthine mimetics using a copper-catalyzed cyclocondensation of bromoaryl guanidines and their inhibition of human dipeptidylpeptidase IV)

RN 918931-39-2 HCAPLUS

CN Benzonitrile, 3-[[2-(3-amino-1-piperidinyl)-6,7-dihydro-6-methyl-7-oxo-1H-imidazo[4,5-d]pyridazin-1-yl]methyl]-, hydrochloride (1:1) (CA INDEX NAME)

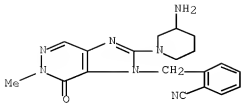


IT 918931-35-8P 918931-40-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of an aminopiperidinyl-substituted fused imidazole as an inhibitor of human dipeptidylpeptidase IV, its selectivity for DPPIV over DPP8, DPP9, and prolyl oligopeptidase, and its stability in the presence of rat plasma)

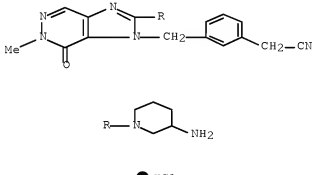
RN 918931-35-8 HCAPLUS

CN Benzonitrile, 2-[[2-(3-amino-1-piperidinyl)-6,7-dihydro-6-methyl-7-oxo-1H-imidazo[4,5-d]pyridazin-1-yl]methyl]-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

RN 918931-40-5 HCAPLUS
CN Benzeneacetonitrile, 3-[[2-(3-amino-1-piperidinyl)-6,7-dihydro-6-methyl-7-oxo-1H-imidazo[4,5-d]pyridazin-1-yl]methyl]-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

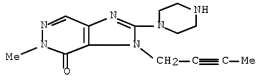
L6 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1138163 HCAPLUS Full-text
DOCUMENT NUMBER: 146:134487
TITLE: Reliable on-line sample preparation of basic compounds from plasma using a reversed phase restricted access media in column-switching LC
AUTHOR(S): Yamamoto, Eiichi; Igarashi, Hatsue; Sato, Yoshiaki; Kushida, Ikuo; Kato, Takashi; Kajima, Takashi; Asakawa, Naoki
CORPORATE SOURCE: Analytical Research Laboratories, Eisai Co. Ltd., Tsukuba, Ibaraki, 300-2635, Japan
SOURCE: Journal of Pharmaceutical and Biomedical Analysis (2006), 42(5), 587-592
CODEN: JPBADA; ISSN: 0731-7085
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We investigated online sample preparation of basic compds. from blood plasma using a methylcellulose-immobilized reversed-phase restricted-access media in column-switching liquid chromatog. (LC). Dilution of the plasma sample with

phosphate buffered saline prevented or delayed the formation of fibrin clots at 4 °C and resulted in reproducible online sample preparation over a 30-h period. The use of an ion-pair reagent in the extraction LC enhanced recoveries of hydrophilic basic compds. The ability of the methods to quantify compds. in plasma were validated and the method was successfully applied to the pharmacokinetic study of a hydrophilic basic compound injected into the bloodstream of rats.

IT 635717-65-6, ER 235516
RL: ANT (Analyte); PKT (Pharmacokinetics); PRP (Properties); ANST (Analytical study); BIOL (Biological study)
(sample preparation of basic compds. from blood plasma using reversed phase LC)

RN 635717-65-6 HCAPLUS

CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-methyl-2-(1-piperazinyl)- (CA INDEX NAME)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:993756 HCAPLUS Full-text

DOCUMENT NUMBER: 146:583

TITLE: E3024, 3-but-2-ynyl-5-methyl-2-piperazin-1-yl-3,5-dihydro-4H-imidazo[4,5-d]pyridazin-4-one tosylate, is a novel, selective and competitive dipeptidyl peptidase-IV inhibitor

AUTHOR(S): Yasuda, Nobuyuki; Nagakura, Tadashi; Inoue, Takashi; Yamazaki, Kazuto; Katsutani, Naruo; Takenaka, Osamu; Clark, Richard; Matsuura, Fumiyoshi; Emori, Eita; Yoshikawa, Seiji; Kira, Kazunobu; Ikuta, Hironori; Okada, Toshimi; Saeki, Takao; Asano, Osamu; Tanaka, Isao

CORPORATE SOURCE: Tsukuba Research Laboratories, Eisai Co., Ltd., Tsukuba, Ibaraki, 300-2635, Japan

SOURCE: European Journal of Pharmacology (2006), 548(1-3), 181-187
CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Dipeptidyl peptidase IV (DPP-IV) inhibitors are expected to become a useful new class of anti-diabetic agent. The aim of the present study is to characterize the in vitro and in vivo profile of E3024, 3-but-2-ynyl-5-methyl-2-piperazin-1-yl-3,5-dihydro-4H-imidazo[4,5- d]pyridazin-4-one tosylate, which is a novel imidazopyridazinone-derived DPP-IV inhibitor. E3024 inhibited recombinant human and mouse DPP-IV with IC50 values of approx. 100 nM. E3024 inhibited DPP-IV in human, mouse, rat and canine plasma with IC50 values of 140 to 400 nM. In contrast, E3024 did not inhibit DPP-8 or DPP-9 activity. Kinetic anal. indicated that E3024 is a competitive DPP-IV inhibitor. In

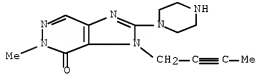
Zucker fa/fa rats, E3024 (1 mg/kg) reduced glucose excursion after glucose load, with increases in plasma insulin and active glucagon-like peptide-1 levels. In fasted rats, this compound did not cause hypoglycemia. In a rat 4-wk toxicol. study, no notable changes were found at doses up to 750 mg/kg. The present preclin. studies indicate that E3024 is a novel selective DPP-IV inhibitor with anti-diabetic effects and a good safety profile.

IT 915132-86-4
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(evaluation of antidiabetic activity, safety, and pharmacokinetics of selective dipeptidyl peptidase-IV inhibitor E3024)

RN 915132-86-4 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-methyl-2-(1-piperazinyl)-, methanesulfonate (1:1) (CA INDEX NAME)

CM 1

CRN 635717-65-6
CMF C14 H18 N6 O



CM 2

CRN 75-75-2
CMF C H4 O3 S

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

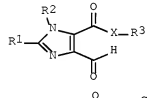
L6 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:1242409 HCAPLUS Full-text
DOCUMENT NUMBER: 144:6797
TITLE: Preparation of 1H-imidazo[4,5-d]pyridazin-4-ols as intermediate products for producing medicaments and pesticides
INVENTOR(S): Eckhardt, Matthias
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

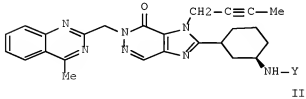
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005110999	A1	20051124	WO 2005-EP4942	20050506
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 102004022970	A1	20051201	DE 2004-102004022970	20040510
CA 2562857	A1	20051124	CA 2005-2562857	20050506
EP 1753729	A1	20070221	EP 2005-736446	20050506
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
JP 2007536325	T	20071213	JP 2007-512042	20050506
US 20050261352	A1	20051124	US 2005-124798	20050509

PRIORITY APPLN. INFO.: DE 2004-102004022970A 20040510
US 2004-576219P P 20040602
WO 2005-EP4942 W 20050506

OTHER SOURCE(S): MARPAT 144:6797
GI



I



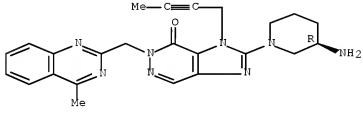
II

AB Title compds. I [R1 = halo; R2 = alkyl with provisos; X = O, S; R3 = H, alkyl with provisos] were prepd as intermediates for producing medicaments or pesticides. For example, TFA mediated deprotection of Boc-amine II (Y = Boc) afforded imidazo[4,5-d]pyridazin-4-ol II (Y = H) in 89% yield.

IT 705279-88-5P, (R)-2-(3-Aminopiperidin-1-yl)-3-(but-2-ynyl)-5-(4-methylquinazolin-2-ylmethyl)-3,5-dihydroimidazo[4,5-d]pyridazin-4-one
705279-97-6P 705279-98-7P 705279-99-8P
705280-19-9P 705280-67-7P 813462-55-4P
855789-80-9P 855789-81-0P 855789-82-1P
869966-01-8P 869966-02-9P 869966-03-0P
869966-04-1P 869966-05-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of imidazo[4,5-d]pyridazin-4-ols as intermediate products for producing medicaments and pesticides)

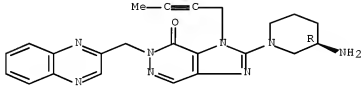
RN 705279-88-5 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(4-methyl-2-quinazolinyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



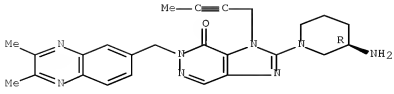
RN 705279-97-6 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-(2-quinoxalinylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.



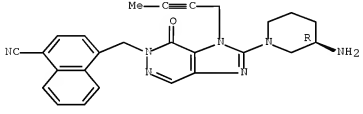
RN 705279-98-7 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-5-[(2,3-dimethyl-6-quinoxalinyl)methyl]-3,5-dihydro- (CA INDEX NAME)

Absolute stereochemistry.



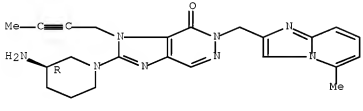
RN 705279-99-8 HCAPLUS
CN 1-Naphthalenecarbonitrile, 4-[[2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.

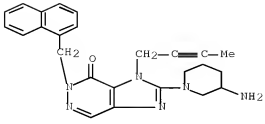


RN 705280-19-9 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(5-methylimidazo[1,2-a]pyridin-2-yl)methyl]- (CA INDEX NAME)

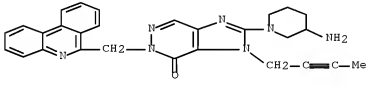
Absolute stereochemistry.



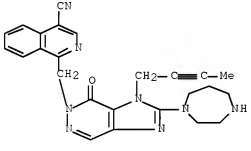
RN 705280-67-7 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3-(2-butyn-1-yl)-3,5-dihydro-5-(1-naphthalenylmethyl)- (CA INDEX NAME)



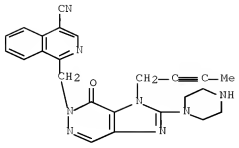
RN 813462-55-4 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3-(2-butyn-1-yl)-3,5-dihydro-5-(6-phenanthridinylmethyl)- (CA INDEX NAME)



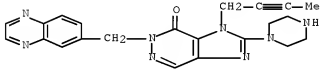
RN 855789-80-9 HCAPLUS
CN 4-Isoquinolinecarbonitrile, 1-[[3-(2-butyn-1-yl)-2-(hexahydro-1H-1,4-diazepin-1-yl)-3,4-dihydro-4-oxo-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]- (CA INDEX NAME)



RN 855789-81-0 HCAPLUS
CN 4-Isoquinolinecarbonitrile, 1-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]- (CA INDEX NAME)

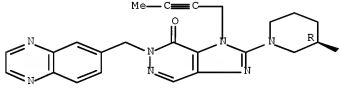


RN 855789-82-1 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-2-(1-piperazinyl)-5-(6-quinoxalinylmethyl)- (CA INDEX NAME)



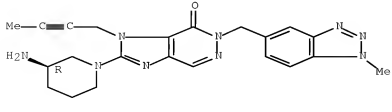
RN 869966-01-8 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-(6-quinoxalinylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.



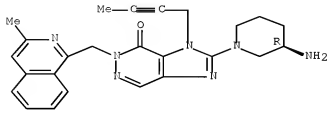
RN 869966-02-9 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(1-methyl-1H-benzotriazol-5-yl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



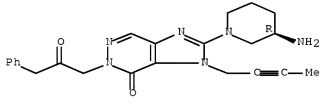
RN 869966-03-0 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(3-methyl-1-isoquinolinyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



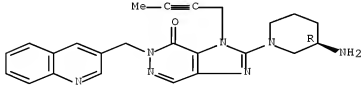
RN 869966-04-1 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-(2-oxo-3-phenylpropyl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 869966-05-2 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-(3-quinolinylmethyl)- (CA INDEX NAME)

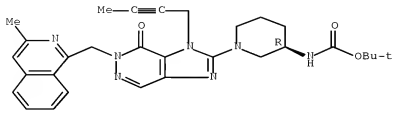
Absolute stereochemistry.



IT 869966-08-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of imidazo[4,5-d]pyridazin-4-ols as intermediate products for producing medicaments and pesticides)
RN 869966-08-5 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-6,7-dihydro-6-[(3-methyl-1-isoquinolinyl)methyl]-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-

piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:570898 HCAPLUS Full-text
DOCUMENT NUMBER: 143:78214
TITLE: Preparation of (homo)piperazinylimidazoyridazinones for treatment of diabetes mellitus.
INVENTOR(S): Himmelsbach, Frank; Hauel, Norbert; Langkopf, Elke; Eckhardt, Matthias; Kauffmann-Hefner, Iris; Tadayyon, Mohammad; Thomas, Leo
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. KG
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005058901	A1	20050630	WO 2004-EP14125	20041211
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10359098	A1	20050728	DE 2003-10359098	20031217
CA 2543074	A1	20050630	CA 2004-2543074	20041211
EP 1742949	A1	20070117	EP 2004-803766	20041211
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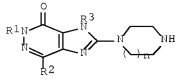
JP 2007513989	T	20070531	JP 2006-544293	20041211
US 20050171093	A1	20050804	US 2004-16176	20041217
US 7217711	B2	20070515		

PRIORITY APPLN. INFO.:			
DE 2003-10359098	A	20031217	
US 2004-538555P	P	20040123	

WO 2004-EP14125 W 20041211

OTHER SOURCE(S): MARPAT 143:78214

GI



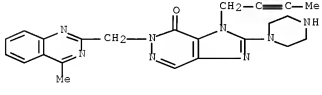
I

AB Title compds. [I; R1 = (substituted) heteroarylalkyl, naphthylalkyl; R2 = H, Me; R3 = 2-butyn-1-yi, 1-buten-1-yl, 2-buten-1-yl, 3-methyl-2-buten-1- yl], were prepared Thus, 2-bromo-3-(2-butyn-1-yl)-5-[(4-methylquinazolin-2-yl)methyl]-3,5-dihydroimidazo[4,5-d]pyridazin-4-one (preparation given) and piperazine were microwaved in DMF at 200° for 5 min. to give 51% 2-(piperazin-1-yl)-3-(2-butyn-1-yl)-5-[(4-methylquinazolin-2-yl)methyl]- 3,5-dihydroimidazo[4,5-d]pyridazin-4-one. The latter inhibited dipeptidylpeptidase-IV with IC50 = 5 nM.

IT 855789-37-6P, 2-(Piperazin-1-yl)-3-(2-butyn-1-yl)-5-[(4-methylquinazolin-2-yl)methyl]-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one 855789-38-7P, 2-([1,4]Diazepan-1-yl)-3-(2-butyn-1-yl)-5-[(4-methylquinazolin-2-yl)methyl]-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one 855789-39-8P, 2-(Piperazin-1-yl)-3-(2-butyn-1-yl)-5-[(4-methylbenzoxazol-2-yl)methyl]-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one 855789-40-1P, 2-([1,4]Diazepan-1-yl)-3-(2-butyn-1-yl)-5-[(4-methylbenzoxazol-2-yl)methyl]-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of (homo)piperazinylimidazoyridazinones for treatment of diabetes mellitus)

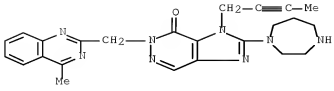
RN 855789-37-6 HCAPLUS

CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-[(4-methyl-2-quinazolinyl)methyl]-2-(1-piperazinyl)- (CA INDEX NAME)

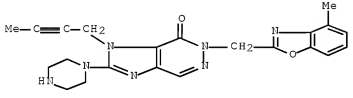


RN 855789-38-7 HCAPLUS

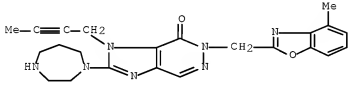
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-2-(hexahydro-1H-1,4-diazepin-1-yl)-3,5-dihydro-5-[(4-methyl-2-quinazolinyl)methyl]- (CA INDEX NAME)



RN 855789-39-8 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-[(4-methyl-2-benzoxazolyl)methyl]-2-(1-piperazinyl)- (CA INDEX NAME)



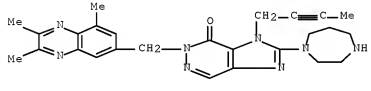
RN 855789-40-1 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-2-(hexahydro-1H-1,4-diazepin-1-yl)-3,5-dihydro-5-[(4-methyl-2-benzoxazolyl)methyl]- (CA INDEX NAME)



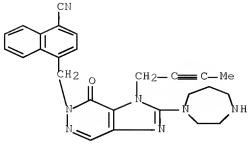
IT 855789-60-5P, 2-([1,4]Diazepan-1-yl)-3-(2-butyn-1-yl)-5-[(2,3,8-trimethyl-quinoxalin-6-yl)methyl]-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one 855789-61-6P, 2-([1,4]Diazepan-1-yl)-3-(2-butyn-1-yl)-5-[(4-cyano-naphthalin-1-yl)methyl]-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one 855789-62-7P, 2-(Piperazin-1-yl)-3-(2-butyn-1-yl)-5-[(4-cyano-naphthalin-1-yl)methyl]-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one 855789-63-8P, 2-(Piperazin-1-yl)-3-(2-butyn-1-yl)-5-[(4-fluoro-naphthalin-1-yl)methyl]-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one 855789-64-9P, 2-([1,4]Diazepan-1-yl)-3-(2-butyn-1-yl)-5-[(4-fluoro-naphthalin-1-yl)methyl]-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one 855789-65-0P, 2-(Piperazin-1-yl)-3-(2-butyn-1-yl)-5-[(4-bromo-naphthalin-1-yl)methyl]-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one 855789-66-1P, 2-([1,4]Diazepan-1-yl)-3-(2-butyn-1-yl)-5-[(4-bromo-naphthalin-1-yl)methyl]-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one 855789-67-2P, 2-(Piperazin-1-yl)-3-(2-butyn-1-yl)-5-[([1,2,4]triazolo[4,3-a]pyridin-3-yl)methyl]-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one 855789-68-3P, 2-(Piperazin-1-yl)-3-(2-butyn-1-yl)-5-[(1-methyl-1H-benzotriazol-5-yl)methyl]-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one 855789-69-4P, 2-([1,4]Diazepan-1-yl)-3-(2-

butyn-1-yl)-5-[(1-methyl-1H-benzotriazol-5-yl)methyl]-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one 855789-71-8P, 2-([1,4]Diazepan-1-yl)-3-(2-butyn-1-yl)-5-[([1,2,4]triazolo[4,3-a]pyridin-3-yl)methyl]-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one 855789-73-0P, 2-(Piperazin-1-yl)-3-(2-butyn-1-yl)-5-[(4-methyl-pyridin-2-yl)methyl]-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one 855789-74-1P, 2-([1,4]Diazepan-1-yl)-3-(2-butyn-1-yl)-5-[(4-methyl-pyridin-2-yl)methyl]-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one 855789-75-2P 855789-76-3P 855789-77-4P, 2-(Piperazin-1-yl)-3-(2-butyn-1-yl)-5-[(3-methyl-isoquinolin-1-yl)methyl]-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one 855789-78-5P, 2-([1,4]Diazepan-1-yl)-3-(2-butyn-1-yl)-5-[(3-methyl-isoquinolin-1-yl)methyl]-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one 855789-79-6P, 2-([1,4]Diazepan-1-yl)-3-(2-butyn-1-yl)-5-[(1,5-naphthyridin-2-yl)methyl]-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one 855789-80-9P, 2-([1,4]Diazepan-1-yl)-3-(2-butyn-1-yl)-5-[(4-cyano-isoquinolin-1-yl)methyl]-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one 855789-81-0P, 2-(Piperazin-1-yl)-3-(2-butyn-1-yl)-5-[(4-cyano-isoquinolin-1-yl)methyl]-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one 855789-82-1P, 2-(Piperazin-1-yl)-3-(2-butyn-1-yl)-5-[(quinoxalin-6-yl)methyl]-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one 855789-83-2P, 2-(Piperazin-1-yl)-3-(2-butyn-1-yl)-5-[(2,3,8-trimethyl-quinoxalin-6-yl)methyl]-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (homo)piperazinylimidazoyridazinones for treatment of diabetes mellitus)

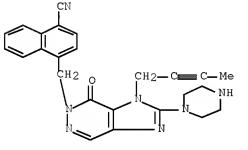
RN 855789-60-5 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-2-(hexahydro-1H-1,4-diazepin-1-yl)-3,5-dihydro-5-[(2,3,8-trimethyl-6-quinoxalinyl)methyl]- (CA INDEX NAME)



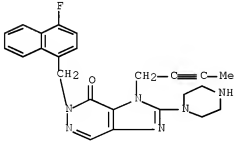
RN 855789-61-6 HCAPLUS
CN 1-Naphthalenecarbonitrile, 4-[[3-(2-butyn-1-yl)-2-(hexahydro-1H-1,4-diazepin-1-yl)-3,4-dihydro-4-oxo-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]- (CA INDEX NAME)



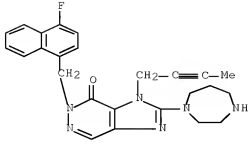
RN 855789-62-7 HCAPLUS
CN 1-Naphthalenecarbonitrile, 4-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]- (CA INDEX NAME)



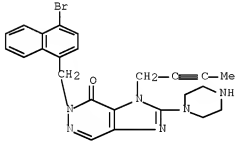
RN 855789-63-8 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-5-[(4-fluoro-1-naphthalenyl)methyl]-3,5-dihydro-2-(1-piperazinyl)- (CA INDEX NAME)



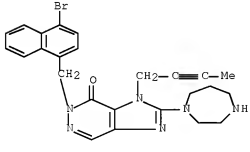
RN 855789-64-9 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-5-[(4-fluoro-1-naphthalenyl)methyl]-2-(hexahydro-1H-1,4-diazepin-1-yl)-3,5-dihydro- (CA INDEX NAME)



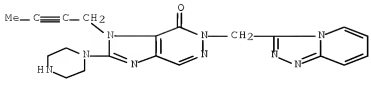
RN 855789-65-0 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 5-[(4-bromo-1-naphthalenyl)methyl]-3-(2-butyn-1-yl)-3,5-dihydro-2-(1-piperazinyl)- (CA INDEX NAME)



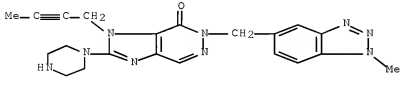
RN 855789-66-1 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 5-[(4-bromo-1-naphthalenyl)methyl]-3-(2-butyn-1-yl)-2-(hexahydro-1H-1,4-diazepin-1-yl)-3,5-dihydro- (CA INDEX NAME)



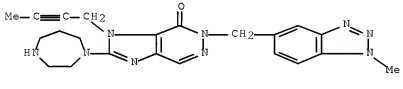
RN 855789-67-2 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-2-(1-piperazinyl)-5-(1,2,4-triazolo[4,3-a]pyridin-3-ylmethyl)- (CA INDEX NAME)



RN 855789-68-3 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-[(1-methyl-1H-benzotriazol-5-yl)methyl]-2-(1-piperazinyl)- (CA INDEX NAME)



RN 855789-69-4 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-2-(hexahydro-1H-1,4-diazepin-1-yl)-3,5-dihydro-5-[(1-methyl-1H-benzotriazol-5-yl)methyl]- (CA INDEX NAME)



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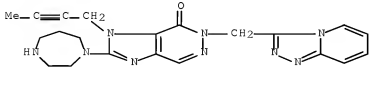
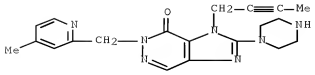
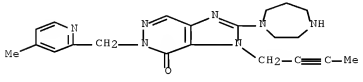
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-2-(hexahydro-1H-1,4-diazepin-1-yl)-3,5-dihydro-5-(1,2,4-triazolo[4,3-a]pyridin-3-ylmethyl)- (CA INDEX NAME)



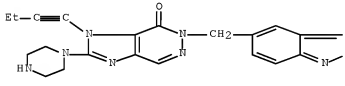
RN 855789-73-0 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-[(4-methyl-2-pyridinyl)methyl]-2-(1-piperazinyl)- (CA INDEX NAME)



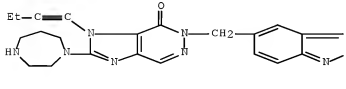
RN 855789-74-1 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-2-(hexahydro-1H-1,4-diazepin-1-yl)-3,5-dihydro-5-[(4-methyl-2-pyridinyl)methyl]- (CA INDEX NAME)



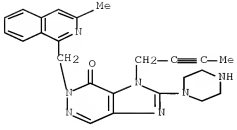
RN 855789-75-2 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 5-(2,1,3-benzothiadiazol-5-ylmethyl)-3-(1-butyn-1-yl)-3,5-dihydro-2-(1-piperazinyl)- (CA INDEX NAME)



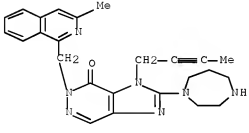
RN 855789-76-3 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 5-(2,1,3-benzothiadiazol-5-ylmethyl)-3-(1-butyn-1-yl)-2-(hexahydro-1H-1,4-diazepin-1-yl)-3,5-dihydro- (CA INDEX NAME)



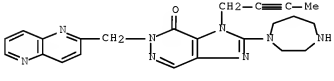
RN 855789-77-4 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-[(3-methyl-1-isoquinolinyl)methyl]-2-(1-piperazinyl)- (CA INDEX NAME)



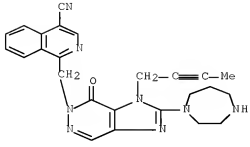
RN 855789-78-5 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-2-(hexahydro-1H-1,4-diazepin-1-yl)-3,5-dihydro-5-[(3-methyl-1-isoquinolinyl)methyl]- (CA INDEX NAME)



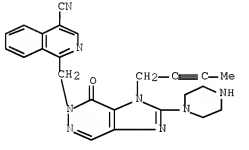
RN 855789-79-6 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-2-(hexahydro-1H-1,4-diazepin-1-yl)-3,5-dihydro-5-(1,5-naphthyridin-2-ylmethyl)- (CA INDEX NAME)



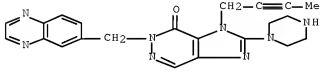
RN 855789-80-9 HCAPLUS
CN 4-Isoquinolinecarbonitrile, 1-[[3-(2-butyn-1-yl)-2-(hexahydro-1H-1,4-diazepin-1-yl)-3,4-dihydro-4-oxo-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]- (CA INDEX NAME)



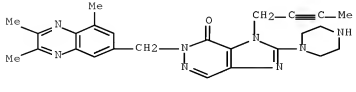
RN 855789-81-0 HCAPLUS
CN 4-Isoquinolinecarbonitrile, 1-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]- (CA INDEX NAME)



RN 855789-82-1 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-2-(1-piperazinyl)-5-(6-quinoxalinylmethyl)- (CA INDEX NAME)



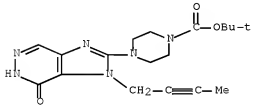
RN 855789-83-2 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-2-(1-piperazinyl)-5-[(2,3,8-trimethyl-6-quinoxalinyl)methyl]- (CA INDEX NAME)



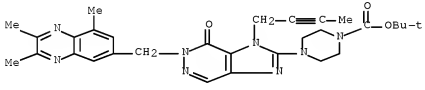
IT 635723-01-2P, 2-(4-tert-Butoxycarbonyl-piperazin-1-yl)-3-(2-butyn-

1-yl)-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one 855789-41-2P,
2-(4-tert-Butoxycarbonyl-piperazin-1-yl)-3-(2-butyn-1-yl)-5-[(2,3,8-trimethyl-quinoxalin-6-yl)methyl]-3,5-dihydro-imidazo[4,5-d]pyridazin-4-one
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (homo)piperazinylimidazoyridazinones for treatment of diabetes mellitus)

RN 635723-01-2 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[1-(2-butyn-1-yl)-6,7-dihydro-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



RN 855789-41-2 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[1-(2-butyn-1-yl)-6,7-dihydro-7-oxo-6-[(2,3,8-trimethyl-6-quinoxalinyl)methyl]-1H-imidazo[4,5-d]pyridazin-2-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:570533 HCAPLUS Full-text
DOCUMENT NUMBER: 143:97364
TITLE: Bicyclic imidazole derivatives, the preparation thereof and their use as pharmaceutical compositions
INVENTOR(S): Himmelsbach, Frank; Langkopf, Elke; Eckhardt, Matthias; Hauel, Norbert; Tadayyon, Mohammad; Thomas, Leo
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany
SOURCE: U.S. Pat. Appl. Publ., 17 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20050143377	A1	20050630	US 2004-18894	20041221
US 7183280	B2	20070227		
DE 10360835	A1	20050721	DE 2003-10360835	20031223
DE 102004046530	A1	20060330	DE 2004-102004046530	20040924
CA 2548323	A1	20050714	CA 2004-2548323	2004121 7
WO 2005063750	A1	20050714	WO 2004-EP14399	2004121 7
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
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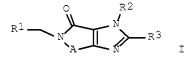
EP 1709049	A1	20061011	EP 2004-804004	2004121 7
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS			
JP 2007515442	T	20070614	JP 2006-546011	2004121 7

PRIORITY APPLN. INFO.: DE 2003-10360835 A 20031223
US 2004-538684P P 20040123
DE 2004-102004046530A 20040924
WO 2004-EP14399 W 2004121 7

OTHER SOURCE(S): CASREACT 143:97364; MARPAT 143:97364

GI



I

AB The present invention relates to bicyclic imidazole compds. of general formula I wherein R1 to R3 and A are defined in claims (an example of a compound of the invention is 1-[(4-methyl-3-oxyquinazolin-2-yl)methyl]-3- methyl-7-(2-butyn-1-yl)-8-((R)-3-aminopiperidin-1-yl)xanthine), , the tautomers, the enantiomers, the stereoisomers, the mixts. thereof and the salts thereof, which have valuable pharmacol. properties, particularly an inhibiting effect on the activity of the enzyme dipeptidylpeptidase-IV (DPP-IV). In addition to the compds., pharmaceutical compns. containing I and a process for preparing I are also claimed. A method of treating a disease chosen from type I and II diabetes mellitus, arthritis, obesity, allograft transplantation and calcitonin-induced osteoporosis using I is also claimed.

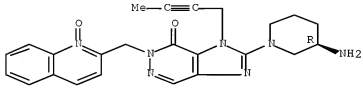
IT 856408-30-5P 856408-31-6P 856408-32-7P
856408-33-8P 856408-34-9P 856408-35-0P
856408-37-2P 856408-38-3P, 2-(Piperazin-1-yl)-3-(2-butyn-1-yl)-5-[(4-methyl-3-oxide-quinazolin-2-yl)methyl]-3,5-dihydroimidazo[4,5-d]pyridazin-4-one
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(candidate drug; preparation of bicyclic imidazole derivs. and their use in pharmaceutical compns. for treating various diseases)

RN 856408-30-5 HCAPLUS

CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(1-oxido-2-quinolinyl)methyl]- (CA INDEX NAME)

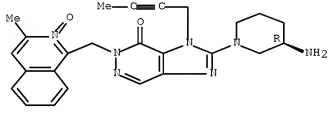
Absolute stereochemistry.



RN 856408-31-6 HCAPLUS

CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(3-methyl-2-oxido-1-isoquinolinyl)methyl]- (CA INDEX NAME)

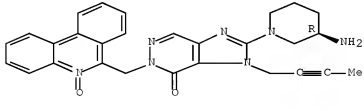
Absolute stereochemistry.



RN 856408-32-7 HCAPLUS

CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(5-oxido-6-phenanthridinyl)methyl]- (CA INDEX NAME)

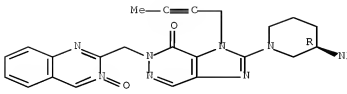
Absolute stereochemistry.



RN 856408-33-8 HCAPLUS

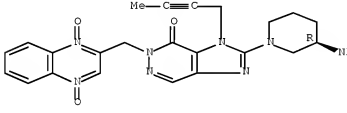
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(3-oxido-2-quinazolinyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



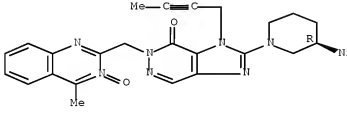
RN 856408-34-9 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-5-[(1,4-dioxido-2-quinoxalinyl)methyl]-3,5-dihydro- (CA INDEX NAME)

Absolute stereochemistry.



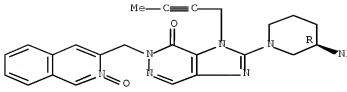
RN 856408-35-0 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(4-methyl-3-oxido-2-quinazolinyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.

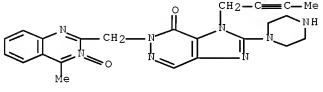


RN 856408-37-2 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(2-oxido-3-isoquinolinyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.

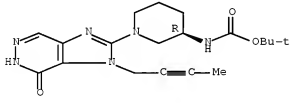


RN 856408-38-3 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-[(4-methyl-3-oxido-2-quinazolinyl)methyl]-2-(1-piperazinyl)- (CA INDEX NAME)



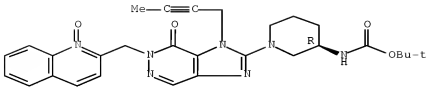
IT 813462-78-1P 856408-11-2P 856408-12-3P
856408-13-4P 856408-14-5P 856408-15-6P
856408-17-8P 856408-19-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of bicyclic imidazole derivs. and their use in pharmaceutical compns. for treating various diseases)
RN 813462-78-1 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-6,7-dihydro-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



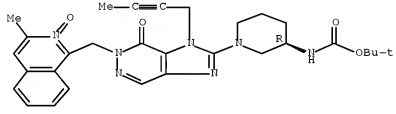
RN 856408-11-2 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-6,7-dihydro-6-[(1-oxido-2-quinolinyl)methyl]-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



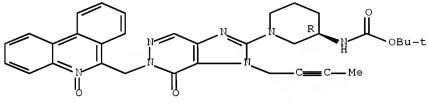
RN 856408-12-3 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-6,7-dihydro-6-[(3-methyl-2-oxido-1-isoquinolinyl)methyl]-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



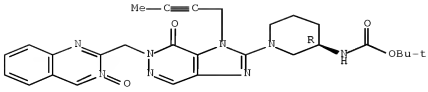
RN 856408-13-4 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-6,7-dihydro-6-[(5-oxido-6-phenanthridinyl)methyl]-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



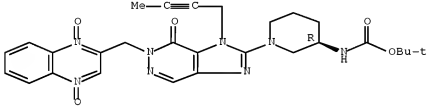
RN 856408-14-5 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-6,7-dihydro-6-[(3-oxido-2-quinazolinyl)methyl]-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



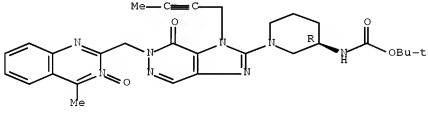
RN 856408-15-6 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-6-[(1,4-dioxido-2-quinoxalinyl)methyl]-6,7-dihydro-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



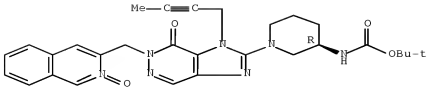
RN 856408-17-8 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-6,7-dihydro-6-[(4-methyl-3-oxido-2-quinazolinyl)methyl]-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 856408-19-0 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-6,7-dihydro-6-[(2-oxido-3-isoquinolinyl)methyl]-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

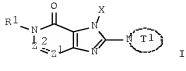


REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:523288 HCAPLUS Full-text
DOCUMENT NUMBER: 143:59991
TITLE: Preparation of fused imidazole derivatives such as dihydroimidazopyridazine, dihydroimidzolpyridine, hypoxanthine, and xanthine derivatives and preventives or therapeutic agents for multiple sclerosis
INVENTOR(S): Muramoto, Kenzo; Yasuda, Nobuyuki
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005053695	A1	20050616	WO 2004-JP14857	20041007
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20070219178	A1	20070920	US 2007-596212	20070112
PRIORITY APPLN. INFO.:			JP 2003-405337 A	20031204
			WO 2004-JP14857 W	20041007

OTHER SOURCE(S): MARPAT 143:59991
GI



I

AB There are provided preventives or therapeutic agents for multiple sclerosis, characterized by containing compds. represented by the following general formula (I) [ring T1 = (un)substituted 4- to 12-membered mono- or dicyclic heterocyclyl containing 1 or 2 N atoms; X = each (un)substituted C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C6-10 aryl, 5- to 10-membered heteroaryl, C6-10 aryl-C1-6 alkyl, or 5- to 10-membered heteroaryl-C1-6 alkyl; the solid line accompanied by a dotted line between Z2 and Z1 = a single or double bond; when the bond is a single bond, Z1 = NR2 and Z2 = CO; when the bond is a double line, Z1, Z2 = N or CR2; R1, R2 = -A0-A1-A2 (wherein A0 = a single bond, (un)substituted C1-6 alkylene; A1 = a single bond, S, O, S(O), S(O)2, O2C, CO2, NRA, CONRA, NRACO, SO2NRA, or NRASO2; A2, RA = H, halo, cyano, each (un)substituted guanidino, C1-6 alkyl, C3-8 cycloalkyl, C3-8 cycloalkenyl, C2-6 alkenyl, C2-6 alkynyl, C6-10 aryl, 5- to 10-membered heteroaryl, 4- to 8-membered heterocyclyl, or 5- to 10-membered heteroaryl-C1-6 alkyl, etc.); when Z2 = CR2, R1 and R2 together form a 5- to 7-membered ring], salts thereof, or hydrates of either. Thus, 7 mg 4-[7-(2-butynyl)-2-chloro-1-(2-cyanobenzyl)-6-oxo-6,7- dihydro-1H-purin-8-yl]piperazine-1-carboxylic acid tert-Bu ester was dissolved in 0.2 mL 1-methyl-2-pyrrolidone, treated with 8 mg 3-hydroxypyridine-2-carboxamide and 8 mg K2CO3, stirred at 100° for 2 h, treated with 1 N aqueous HCl, and extracted with EtOAc. The EtOAc extract was concentrated, dissolved in CF3CO2H, and concentrated to give, after purification using reversed-phase HPLC, 3-[[7-(2-butynyl)-1-(2-cyanobenzyl)-6-oxo-8- (piperazin-1-yl)-6,7-dihydro-1H-purin-2-yl]oxy]pyridine-2-carboxamide trifluoroacetate (II). II showed IC50 of 0.000890 μM against dipeptidyl peptidase IV (DPPIV). 7-(2-Butynyl)-1,3-dimethyl-8-(piperazin- 1-yl)-3,7-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione, 2-[[7-(2-butynyl)-1-methyl-6-oxo-8-(piperazin-1-yl)-6,7-dihydro-1H-purin-2- yl]oxy]benzamide, and 2-(3-aminopiperidin-1-yl)-3-(2-butynyl)-5-methyl-3,5- dihydroimidazo[4,5-d]pyridazin-4-one trifluoroacetate inhibited the onset of allergic encephalomyelitis (EAE) in mice of human multiple sclerosis model.

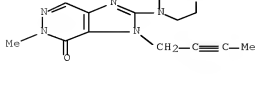
IT 635717-65-6P, 3-(2-Butynyl)-5-methyl-2-(piperazin-1-yl)-3,5-dihydroimidazo[4,5-d]pyridazin-4-one 635720-65-9P, 2-[[3-(2-Butynyl)-4-oxo-2-(piperazin-1-yl)-3,4-dihydroimidazo[4,5-d]pyridazin-5-yl]methyl]benzonitrile 854279-13-3P 854279-14-4P 854279-15-5P 854279-17-7P 854279-18-8P 854279-24-6P 854279-25-7P 854279-26-8P 854279-27-9P 854279-28-0P 854279-29-1P 854279-30-4P 854279-31-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

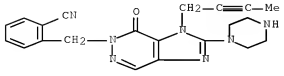
(preparation of fused imidazole derivs. such as dihydroimidazopyridazine, dihydroimidzolpyridine, hypoxanthine, and xanthine derivs. and preventives or therapeutic agents for multiple sclerosis)

RN 635717-65-6 HCAPLUS

CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-methyl-2-(1-piperazinyl)- (CA INDEX NAME)



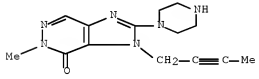
RN 635720-65-9 HCAPLUS
CN Benzonitrile, 2-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]- (CA INDEX NAME)



RN 854279-13-3 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-methyl-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 635717-65-6
CMF C14 H18 N6 O



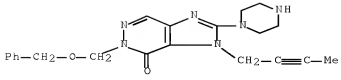
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 854279-14-4 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-[(phenylmethoxy)methyl]-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 635717-67-8
CMF C21 H24 N6 O2



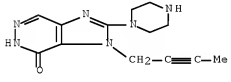
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 854279-15-5 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 635717-69-0
CMF C13 H16 N6 O



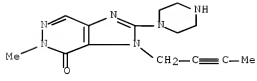
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 854279-17-7 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-methyl-2-(1-piperazinyl)-, 4-methylbenzenesulfonate (1:?) (CA INDEX NAME)

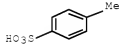
CM 1

CRN 635717-65-6
CMF C14 H18 N6 O



CM 2

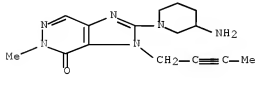
CRN 104-15-4
CMF C7 H8 O3 S



RN 854279-18-8 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3-(2-butyn-1-yl)-3,5-dihydro-5-methyl-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 635717-75-8
CMF C15 H20 N6 O



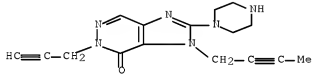
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 854279-24-6 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-2-(1-piperazinyl)-5-(2-propyn-1-yl)-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 635720-47-7
CMF C16 H18 N6 O



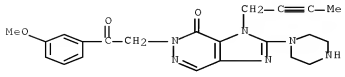
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 854279-25-7 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-[2-(3-methoxyphenyl)-2-oxoethyl]-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 635720-63-7
CMF C22 H24 N6 O3



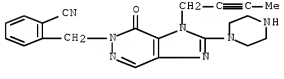
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 854279-26-8 HCAPLUS
CN Benzonitrile, 2-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 635720-65-9
CMF C21 H21 N7 O



CM 2

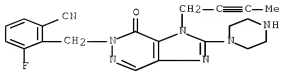
CRN 76-05-1
CMF C2 H F3 O2

RN 854279-27-9 HCAPLUS
CN Benzonitrile, 2-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-3-fluoro-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 635721-29-8

CMF C21 H20 F N7 O



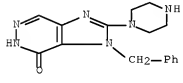
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 854279-28-0 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3,5-dihydro-3-(phenylmethyl)-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 635721-53-8
CMF C16 H18 N6 O



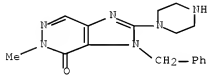
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 854279-29-1 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3,5-dihydro-5-methyl-3-(phenylmethyl)-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 635721-55-0
CMF C17 H20 N6 O



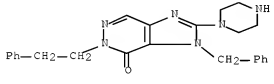
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 854279-30-4 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3,5-dihydro-5-(2-phenylethyl)-3-(phenylmethyl)-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 635721-59-4
CMF C24 H26 N6 O



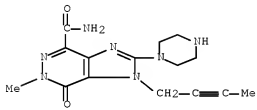
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 854279-31-5 HCAPLUS
CN 1H-Imidazo[4,5-d]pyridazine-4-carboxamide, 1-(2-butyn-1-yl)-6,7-dihydro-6-methyl-7-oxo-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 635722-01-9
CMF C15 H19 N7 O2



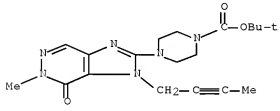
CM 2

CRN 76-05-1
CMF C2 H F3 O2

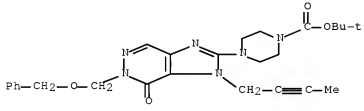
IT 635722-47-3P, 4-[1-(2-Butynyl)-6-methyl-7-oxo-6,7-dihydro-1H-imidazo[4,5-d]pyridazin-2-yl]piperazine-1-carboxylic acid tert-butyl ester 635722-78-0P, 4-[6-Benzyloxymethyl-1-(2-butynyl)-7-oxo-6,7-dihydro-1H-imidazo[4,5-d]pyridazin-2-yl]piperazine-1-carboxylic acid tert-butyl ester 635723-01-2P, 4-[1-(2-Butynyl)-7-oxo-6,7-dihydro-1H-imidazo[4,5-d]pyridazin-2-yl]piperazine-1-carboxylic acid tert-butyl ester 635722-02-3P, 4-(1-Benzyl-6-benzyloxymethyl-7-oxo-6,7-dihydro-1H-imidazo[4,5-d]pyridazin-2-yl)piperazine-1-carboxylic acid tert-butyl ester 635723-03-4P, 4-(1-Benzyl-7-oxo-6,7-dihydro-1H-imidazo[4,5-d]pyridazine-2-yl)piperazine-1-carboxylic acid tert-butyl ester 635723-14-7P, 4-[1-(2-Butynyl)-4-carbamoyl-6-methyl-7-oxo-6,7-dihydro-1H-imidazo[4,5-d]pyridazin-2-yl]piperazine-1-carboxylic acid tert-butyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(preparation of fused imidazole derivs. such as dihydroimidazopyridazine, dihydroimidzolpyridine, hypoxanthine, and xanthine derivs. and preventives or therapeutic agents for multiple sclerosis)

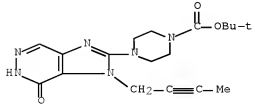
RN 635722-47-3 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[1-(2-butyn-1-yl)-6,7-dihydro-6-methyl-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



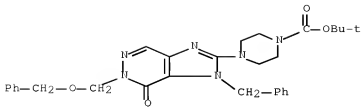
RN 635722-78-0 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[1-(2-butyn-1-yl)-6,7-dihydro-7-oxo-6-[(phenylmethoxy)methyl]-1H-imidazo[4,5-d]pyridazin-2-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



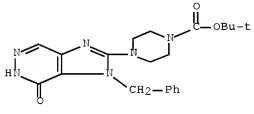
RN 635723-01-2 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[1-(2-butyn-1-yl)-6,7-dihydro-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



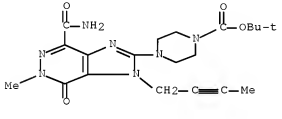
RN 635723-02-3 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[6,7-dihydro-7-oxo-6-[(phenylmethoxy)methyl]-1-(phenylmethyl)-1H-imidazo[4,5-d]pyridazin-2-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



RN 635723-03-4 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[6,7-dihydro-7-oxo-1-(phenylmethyl)-1H-imidazo[4,5-d]pyridazin-2-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



RN 635723-14-7 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4-(aminocarbonyl)-1-(2-butyn-1-yl)-6,7-dihydro-6-methyl-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	2004:1127381 HCAPLUS Full-text
DOCUMENT NUMBER:	142:74585
TITLE:	Preparation of imidazopyridazinones and related compounds as dipeptidyl peptidase IV (DPP-IV) inhibitors for the treatment of diabetes
INVENTOR(S):	Eckhardt, Matthias; Hauel, Norbert; Langkopf, Elke; Himmelsbach, Frank; Kauffmann-Hefner, Iris; Tadayyon, Mohammad; Mark, Michael
PATENT ASSIGNEE(S):	Boehringer Ingelheim International GmbH, Germany; Boehringer Ingelheim Pharma GmbH & Co. Kg
SOURCE:	PCT Int. Appl., 106 pp.

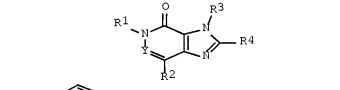
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004111051	A1	20041223	WO 2004-EP6303	20040611
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10327439	A1	20050105	DE 2003-10327439	20030618
US 20050026921	A1	20050203	US 2004-865719	20040610
CA 2529729	A1	20041223	CA 2004-2529729	20040611
EP 1641799	A1	20060405	EP 2004-736644	20040611
EP 1641799	B1	20080312		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
JP 2006527717	T	20061207	JP 2006-515894	20040611
AT 388952	T	20080315	AT 2004-736644	20040611

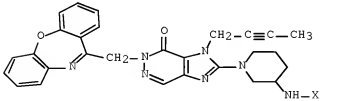
PRIORITY APPLN. INFO.:

DE 2003-10327439	A	20030618
US 2003-487309P	P	20030715
WO 2004-EP6303	W	20040611

OTHER SOURCE(S): MARPAT 142:74585
GI



I



II

AB Title compds. I [R1 = alkyl substituted 3,4-dihydroquinolinyl, 3,4-dihydroisoquinolinyl, 1,4-dihydroquinazolinyl, etc.; R2 = H, F, Cl, etc.; R3 = (un)substituted alkyl, e.g., cycloalkyl, cycloalkenyl, aryl, etc.; R4 = (un)substituted azetidin-1-yl, pyrrolidin-1-yl; Y = N, C-R5; R5 = H, alkyl]

and their pharmaceutically acceptable salts and formulations were prepared For example, TFA mediated deprotection of Boc-amine II (X = Boc) afforded claimed imidazopyridazinone II (X = H) in 63% yield. In dipeptidyl peptidase IV (DPP-IV) inhibition assays, 8-examples of compds. I exhibited IC50 values ranging from 3-58 nM, e.g., the IC50 value of imidazopyridazinone II (X = H) was 14 nM. Compds. I are claimed to be useful for the treatment of type I and type II diabetes mellitus.

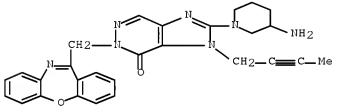
IT 813462-54-3P 813462-55-4P 813462-56-5P
813462-57-6P 813462-58-7P 813462-59-8P
813462-60-1P 813462-61-2P 813462-62-3P
813462-63-4P 813462-64-5P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of imidazopyridazinones and related compds. as dipeptidyl peptidase IV (DPP-IV) inhibitors for the treatment of diabetes)

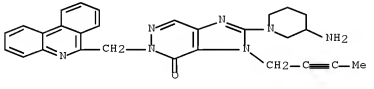
RN 813462-54-3 HCAPLUS

CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3-(2-butyn-1-yl)-5-(dibenz[b,f][1,4]oxazepin-11-ylmethyl)-3,5-dihydro- (CA INDEX NAME)



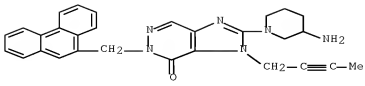
RN 813462-55-4 HCAPLUS

CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3-(2-butyn-1-yl)-3,5-dihydro-5-(6-phenanthridinylmethyl)- (CA INDEX NAME)



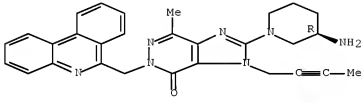
RN 813462-56-5 HCAPLUS

CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3-(2-butyn-1-yl)-3,5-dihydro-5-(9-phenanthrenylmethyl)- (CA INDEX NAME)



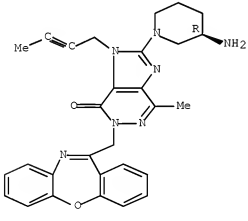
RN 813462-57-6 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-7-methyl-5-(6-phenanthridinylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.



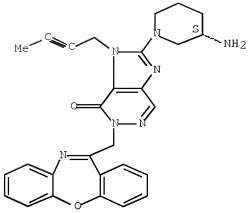
RN 813462-58-7 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-5-(dibenz[b,f][1,4]oxazepin-11-ylmethyl)-3,5-dihydro-7-methyl- (CA INDEX NAME)

Absolute stereochemistry.



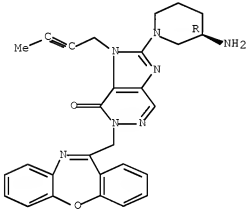
RN 813462-59-8 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3S)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-5-(dibenz[b,f][1,4]oxazepin-11-ylmethyl)-3,5-dihydro- (CA INDEX NAME)

Absolute stereochemistry.



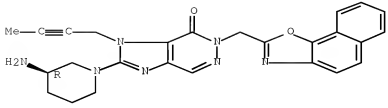
RN 813462-60-1 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-5-(dibenz[b,f][1,4]oxazepin-11-ylmethyl)-3,5-dihydro- (CA INDEX NAME)

Absolute stereochemistry.



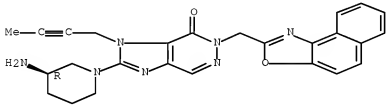
RN 813462-61-2 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-(naphth[2,1-d]oxazol-2-ylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.



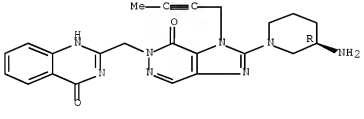
RN 813462-62-3 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-(naphth[1,2-d]oxazol-2-ylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 813462-63-4 HCAPLUS
CN 4(3H)-Quinazolinone, 2-[[2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.

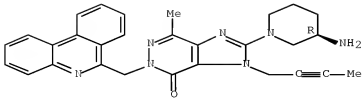


RN 813462-64-5 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-7-methyl-5-(6-phenanthridinylmethyl)-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 813462-57-6
CMF C29 H29 N7 O

Absolute stereochemistry.

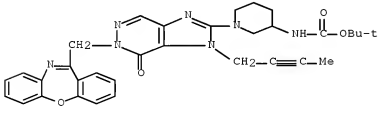


CM 2

CRN 76-05-1
CMF C2 H F3 O2

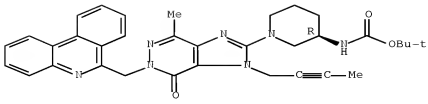
IT 813462-65-6P 813462-66-7P 813462-67-8P
813462-71-4P 813462-72-5P 813462-73-6P
813462-74-7P 813462-75-8P 813462-76-9P
813462-77-0P 813462-78-1P 813462-87-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of imidazopyridazinones and related compds. as dipeptidyl peptidase IV (DPP-IV) inhibitors for the treatment of diabetes)

RN 813462-65-6 HCAPLUS
CN Carbamic acid, [1-[1-(2-butynyl)-6-(dibenz[b,f][1,4]oxazepin-11-ylmethyl)-6,7-dihydro-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



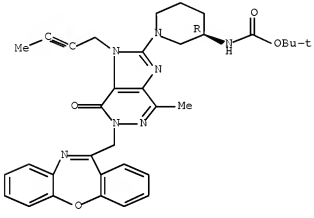
RN 813462-66-7 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-6,7-dihydro-4-methyl-7-oxo-6-(6-phenanthridinylmethyl)-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 813462-67-8 HCAPLUS
CN Carbamic acid, N-[(3R)-1-[1-(2-butyn-1-yl)-6-(dibenz[b,f][1,4]oxazepin-11-ylmethyl)-6,7-dihydro-4-methyl-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)

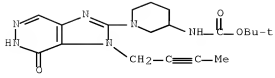
Absolute stereochemistry.



RN 813462-71-4 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-6-(cyanomethyl)-6,7-dihydro-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

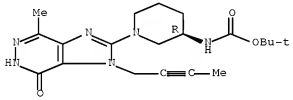
Absolute stereochemistry.

RN 813462-72-5 HCAPLUS
CN Carbamic acid, N-[1-[1-(2-butyn-1-yl)-6,7-dihydro-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



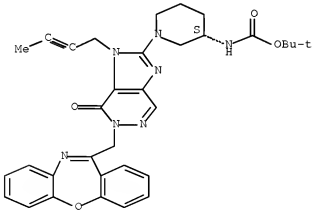
RN 813462-73-6 HCAPLUS
CN Carbamic acid, N-[(3R)-1-[1-(2-butyn-1-yl)-6,7-dihydro-4-methyl-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (CA INDEX NAME)

Absolute stereochemistry.



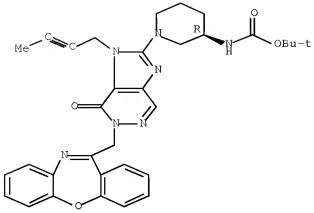
RN 813462-74-7 HCAPLUS
CN Carbamic acid, [(3S)-1-[1-(2-butynyl)-6-(dibenz[b,f][1,4]oxazepin-11-ylmethyl)-6,7-dihydro-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



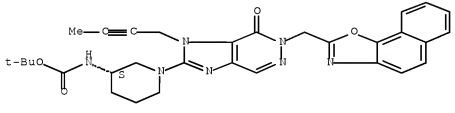
RN 813462-75-8 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-6-(dibenz[b,f][1,4]oxazepin-11-ylmethyl)-6,7-dihydro-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



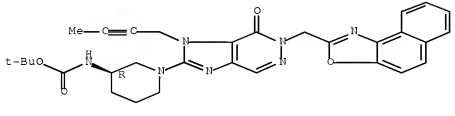
RN 813462-76-9 HCAPLUS
CN Carbamic acid, [(3S)-1-[1-(2-butynyl)-6,7-dihydro-6-(naphth[2,1-d]oxazol-2-ylmethyl)-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



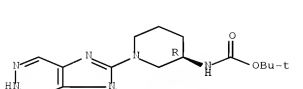
RN 813462-77-0 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-6,7-dihydro-6-(naphth[1,2-d]oxazol-2-ylmethyl)-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



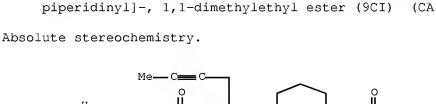
RN 813462-78-1 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-6,7-dihydro-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 813462-87-2 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-6-[(1,4-dihydro-4-oxo-2-quinazolinyl)methyl]-6,7-dihydro-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:493705 HCAPLUS Full-text
DOCUMENT NUMBER: 141:54352
TITLE: Production and use of novel substituted imidazopyridinones and imidazopyridazones as medicaments
INVENTOR(S): Hauel, Norbert; Himmelsbach, Frank; Langkopf, Elke; Eckhardt, Matthias; Maier, Roland; Mark, Michael; Tadayyon, Mohammad; Kauffmann-Hefner, Iris
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

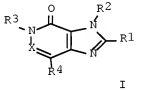
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004050658	A1	20040617	WO 2003-EP13648	20031203
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,				

LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO,
NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10256264	A1	20040624	DE 2002-10256264		20021203
DE 10309927	A1	20040916	DE 2003-10309927		20030307
US 20050020574	A1	20050127	US 2003-726214		20031202
US 7109192	B2	20060919			
CA 2508233	A1	20040617	CA 2003-2508233		20031203
AU 2003293757	A1	20040623	AU 2003-293757		20031203
EP 1569936	A1	20050907	EP 2003-789123		20031203
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2006514980	T	20060518	JP 2004-570687		20031203
PRIORITY APPLN. INFO.:			DE 2002-10256264	A	20021203
			DE 2003-10309927	A	20030307
			US 2002-437438P	P	20021230
			US 2003-456598P	P	20030321
			WO 2003-EP13648	W	20031203

OTHER SOURCE(S): MARPAT 141:54352

GI



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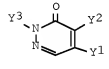

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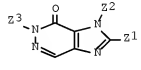


III

AB The invention relates to substituted imidazo-pyridinones and imidazo-pyridazinones I [R1 = 5- to 7-membered cycloalkylenimino (optionally substituted with C1-3-alkyl), 6- to 7-membered cycloalkylenimino (4-methylene substituted, to 7-membered cycloalkylamino, etc.; R2 = CH2Ph (F-, Cl-, Br-, CN-substituted Ph), (un)branched C3-8-alkenyl, C3-5-alkynyl, C3-7-cycloalkylmethyl, C5-7-cycloalkylmethyl, urylmethyl, thienylmethyl, pyrrolylmethyl, thiazolylmethyl, ; R3 = (un)branched C1-6-alkyl, C1-6-haloalkyl, C1-6-cyanoalkyl, CHMePh, CH2CH(OH)Ph, CH2COPh (optionally substituted Ph), 3-methyl-2-oxo-2,3- dihydrobenzoxazolyl)carbonylmethyl, thienylcarbonylmethyl, mono- or bicyclic heteroaryl-(C1-6-alkyl); R4 = H, C1-3-alkyl; X = N, CR5; R5 = H, Me; etc.], the tautomers thereof, the stereoisomers thereof, the mixts. thereof and the salts thereof, which have valuable pharmacol. properties, especially an inhibitory effect on the activity of the enzyme dipeptidylpeptidase-IV (DPP-IV). Thus, I·HCl [R1 = 3-aminopiperidino, R2 = 2-butynyl, R3 = (1-naphthyl)methyl, R4 = H, X = N] was

prepared from 4,5-dichloro-3-hydroxy-2H-pyridazine (II; Y1 = Y2 = Cl, Y3 = H) via N-alkylation with 1-(chloromethyl)naphthalene to give II [Y1 = Y2 = Cl, Y3 = (1-naphthyl)methyl] , hydrolysis-nitration to II [Y1 = OH, Y2 = NO2, Y3 = (1-naphthyl)methyl], amination to give II [Y1 = NH2, Y2 = NO2, Y3 = (1-naphthyl)methyl], reduction to the 4,5-diamino derivative, cyclocondensation with thiocarbonyldiimidazole to give imidazopyridazone III [Z1 = SH, Z2 = H, Z3 = (1-naphthyl)methyl], S-methylation to III [Z1 = SMe, Z2 = H, Z3 = (1-naphthyl)methyl], N-alkylation with BrCH2C.tplbond.CMe to give III [Z1 = SMe, Z2 = CH2C.tplbond.CMe, Z3 = (1-naphthyl)methyl]; S-oxidation to give III [Z1 = SO2Me, Z2 = CH2C.tplbond.CMe, Z3 = (1-naphthyl)methyl],, amination with 3-(Boc-amino)piperidine and deprotection. The inhibitory effect of I [R1 = 3-aminopiperidino, R2 = 2-butynyl, R3 = (1-naphthyl)methyl, R4 = H] on the activity of the enzyme dipeptidylpeptidase-IV (DPP-IV) was tested [IC50 = 13 nM]. Formulations containing I in the forms of dragees, tablets, ampuls, hard-gel capsules, suppositories and suspensions are presented.

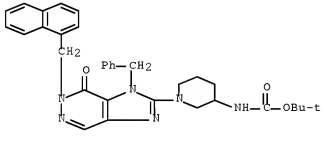
IT 705280-44-0P 705280-47-3P 705280-64-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and N-deprotection of; preparation and use of novel substituted imidazopyridinones and imidazopyridazones as inhibitors of dipeptidylpeptidase IV)

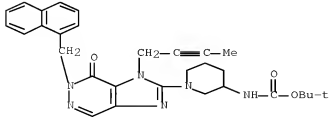
RN 705280-44-0 HCAPLUS

CN Carbamic acid, [1-[6,7-dihydro-6-(1-naphthalenylmethyl)-7-oxo-1-(phenylmethyl)-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



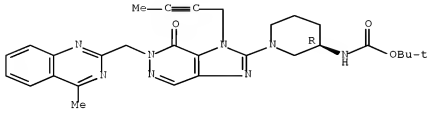
RN 705280-47-3 HCAPLUS

CN Carbamic acid, [1-[1-(2-butynyl)-6,7-dihydro-6-(1-naphthalenylmethyl)-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 705280-64-4 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-6,7-dihydro-6-[(4-methyl-2-quinazolinyl)methyl]-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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705279-96-5P 705279-97-6P 705279-98-7P
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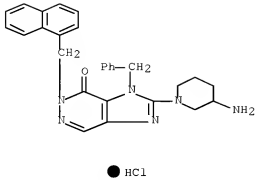
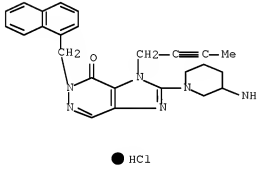
705280-73-5P 705280-74-6P 705280-75-7P
705280-76-8P 705280-77-9P 705280-78-0P
705280-79-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and use of novel substituted imidazopyridinones and imidazopyridazones as inhibitors of dipeptidylpeptidase IV)

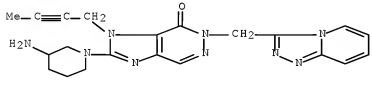
RN 705279-79-4 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3,5-dihydro-5-(1-naphthalenylmethyl)-3-(phenylmethyl)-, hydrochloride (1:1) (CA INDEX NAME)



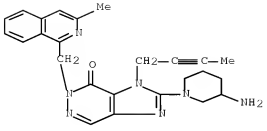
RN 705279-80-7 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3-(2-butyn-1-yl)-3,5-dihydro-5-(1-naphthalenylmethyl)-, hydrochloride (1:1) (CA INDEX NAME)



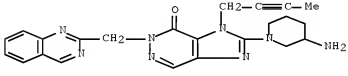
RN 705279-83-0 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3-(2-butyn-1-yl)-3,5-dihydro-5-(1,2,4-triazolo[4,3-a]pyridin-3-ylmethyl)- (CA INDEX NAME)



RN 705279-84-1 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3-(2-butyn-1-yl)-3,5-dihydro-5-[(3-methyl-1-isoquinolinyl)methyl]- (CA INDEX NAME)

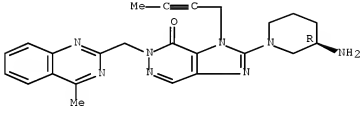


RN 705279-87-4 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3-(2-butyn-1-yl)-3,5-dihydro-5-(2-quinazolinylmethyl)- (CA INDEX NAME)



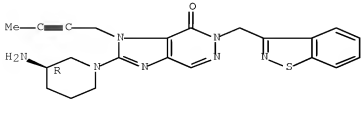
RN 705279-88-5 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(4-methyl-2-quinazolinyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



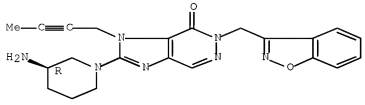
RN 705279-89-6 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-5-(1,2-benzisothiazol-3-ylmethyl)-3-(2-butyn-1-yl)-3,5-dihydro- (CA INDEX NAME)

Absolute stereochemistry.



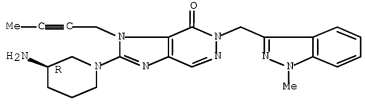
RN 705279-90-9 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-5-(1,2-benzisoxazol-3-ylmethyl)-3-(2-butyn-1-yl)-3,5-dihydro- (CA INDEX NAME)

Absolute stereochemistry.

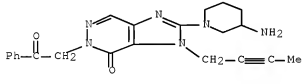


RN 705279-92-1 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(1-methyl-1H-indazol-3-yl)methyl]- (CA INDEX NAME)

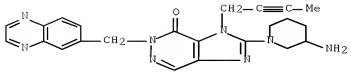
Absolute stereochemistry.



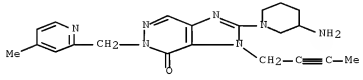
RN 705279-93-2 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3-(2-butyn-1-yl)-3,5-dihydro-5-(2-oxo-2-phenylethyl)- (CA INDEX NAME)



RN 705279-94-3 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3-(2-butyn-1-yl)-3,5-dihydro-5-(6-quinoxalinylmethyl)- (CA INDEX NAME)

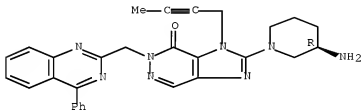


RN 705279-95-4 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3-(2-butyn-1-yl)-3,5-dihydro-5-[(4-methyl-2-pyridinyl)methyl]- (CA INDEX NAME)



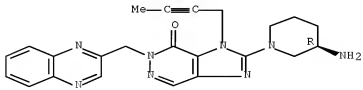
RN 705279-96-5 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(4-phenyl-2-quinazolinyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



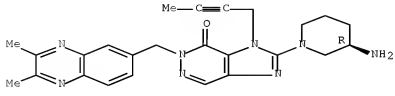
RN 705279-97-6 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-(2-quinoxalinylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.



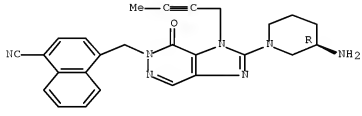
RN 705279-98-7 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-5-[(2,3-dimethyl-6-quinoxalinyl)methyl]-3,5-dihydro- (CA INDEX NAME)

Absolute stereochemistry.

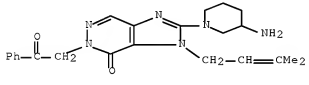


RN 705279-99-8 HCAPLUS
CN 1-Naphthalenecarbonitrile, 4-[[2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.

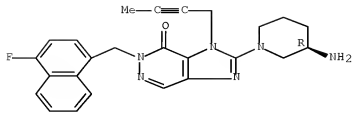


RN 705280-01-9 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3,5-dihydro-3-(3-methyl-2-buten-1-yl)-5-(2-oxo-2-phenylethyl)- (CA INDEX NAME)



RN 705280-03-1 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-5-[(4-fluoro-1-naphthalenyl)methyl]-3,5-dihydro-, hydrochloride (1:1) (CA INDEX NAME)

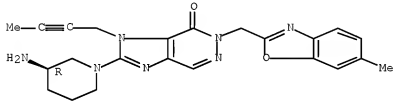
Absolute stereochemistry.



● HCl

RN 705280-04-2 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(6-methyl-2-benzoxazolyl)methyl]-, hydrochloride (1:1) (CA INDEX NAME)

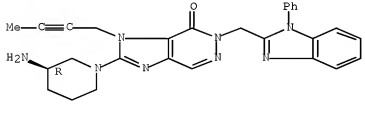
Absolute stereochemistry.



● HCl

RN 705280-05-3 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(1-phenyl-1H-benzimidazol-2-yl)methyl]-, hydrochloride (1:1) (CA INDEX NAME)

Absolute stereochemistry.

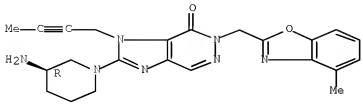


● HCl

RN 705280-06-4 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(4-methyl-2-benzoxazolyl)methyl]-,

hydrochloride (1:1) (CA INDEX NAME)

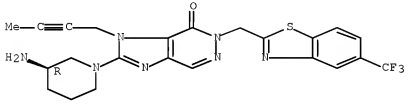
Absolute stereochemistry.



● HCl

RN 705280-07-5 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[[5-(trifluoromethyl)-2-benzothiazolyl]methyl]-, hydrochloride (1:1) (CA INDEX NAME)

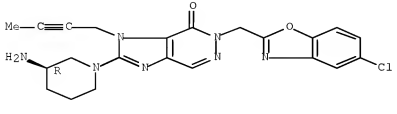
Absolute stereochemistry.



● HCl

RN 705280-08-6 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-5-[(5-chloro-2-benzoxazolyl)methyl]-3,5-dihydro-, hydrochloride (1:1) (CA INDEX NAME)

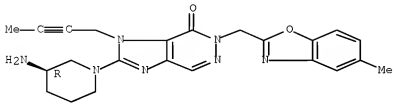
Absolute stereochemistry.



● HCl

RN 705280-09-7 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(5-methyl-2-benzoxazolyl)methyl]-, hydrochloride (1:1) (CA INDEX NAME)

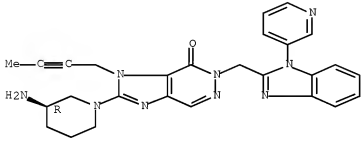
Absolute stereochemistry.



● HCl

RN 705280-10-0 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[[1-(3-pyridinyl)-1H-benzimidazol-2-yl]methyl]-, hydrochloride (1:1) (CA INDEX NAME)

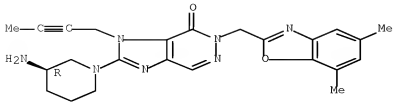
Absolute stereochemistry.



● HCl

RN 705280-11-1 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-5-[(5,7-dimethyl-2-benzoxazolyl)methyl]-3,5-dihydro-, hydrochloride (1:1) (CA INDEX NAME)

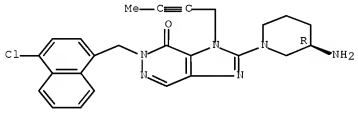
Absolute stereochemistry.



● HCl

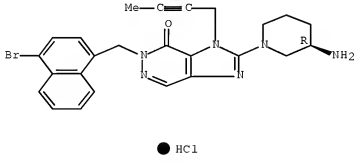
RN 705280-12-2 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-5-[(4-chloro-1-naphthalenyl)methyl]-3,5-dihydro- (CA INDEX NAME)

Absolute stereochemistry.



RN 705280-13-3 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-5-[(4-bromo-1-naphthalenyl)methyl]-3-(2-butyn-1-yl)-3,5-dihydro-, hydrochloride (1:1) (CA INDEX NAME)

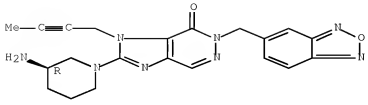
Absolute stereochemistry.



● HCl

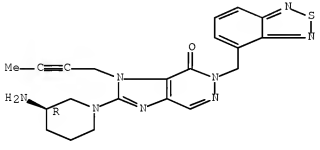
RN 705280-14-4 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-5-(2,1,3-benzoxadiazol-5-ylmethyl)-3-(2-butyn-1-yl)-3,5-dihydro- (CA INDEX NAME)

Absolute stereochemistry.



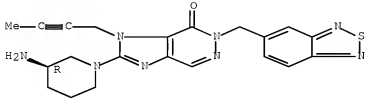
RN 705280-15-5 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-5-(2,1,3-benzothiadiazol-4-ylmethyl)-3-(2-butyn-1-yl)-3,5-dihydro- (CA INDEX NAME)

Absolute stereochemistry.



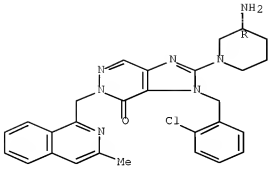
RN 705280-16-6 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-5-(2,1,3-benzothiadiazol-5-ylmethyl)-3-(2-butyn-1-yl)-3,5-dihydro- (CA INDEX NAME)

Absolute stereochemistry.



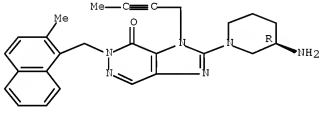
RN 705280-17-7 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-[(2-chlorophenyl)methyl]-3,5-dihydro-5-[(3-methyl-1-isoquinolinyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



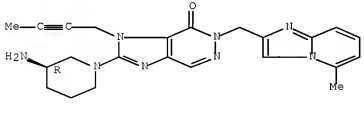
RN 705280-18-8 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(2-methyl-1-naphthalenyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



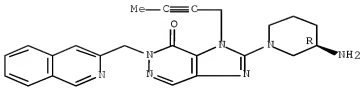
RN 705280-19-9 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(5-methylimidazo[1,2-a]pyridin-2-yl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



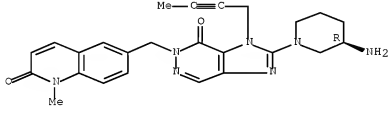
RN 705280-20-2 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-(3-isoquinolinylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.



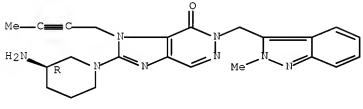
RN 705280-21-3 HCAPLUS
CN 2(1H)-Quinolinone, 6-[[2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-1-methyl- (CA INDEX NAME)

Absolute stereochemistry.



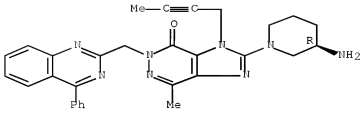
RN 705280-22-4 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(2-methyl-2H-indazol-3-yl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



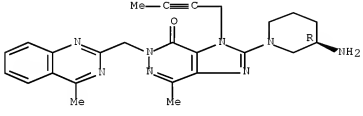
RN 705280-23-5 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-7-methyl-5-[(4-phenyl-2-quinazolinyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



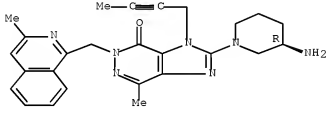
RN 705280-24-6 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-7-methyl-5-[(4-methyl-2-quinazolinyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



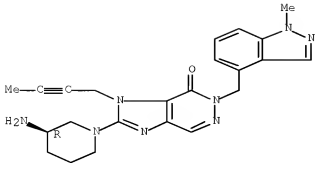
RN 705280-25-7 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-7-methyl-5-[(3-methyl-1-isoquinolinyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



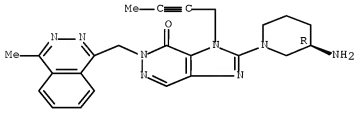
RN 705280-26-8 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(1-methyl-1H-indazol-4-yl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



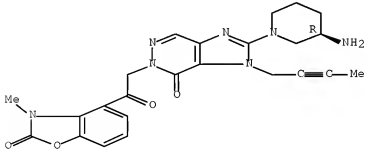
RN 705280-27-9 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(4-methyl-1-phthalazinyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



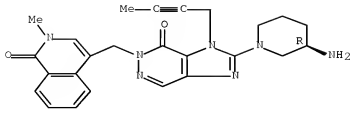
RN 705280-28-0 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-5-[2-(2,3-dihydro-3-methyl-2-oxo-4-benzoxazolyl)-2-oxoethyl]-3,5-dihydro- (CA INDEX NAME)

Absolute stereochemistry.



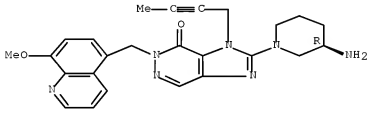
RN 705280-29-1 HCAPLUS
CN 1(2H)-Isoquinolinone, 4-[[2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-2-methyl- (CA INDEX NAME)

Absolute stereochemistry.



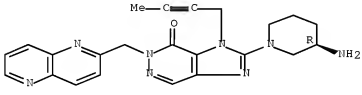
RN 705280-30-4 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(8-methoxy-5-quinolinyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



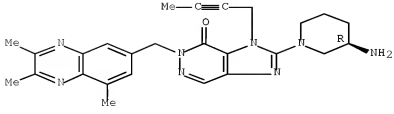
RN 705280-31-5 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-(1,5-naphthyridin-2-ylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.



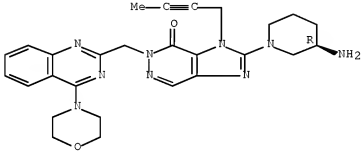
RN 705280-32-6 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(2,3,8-trimethyl-6-quinoxalinyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



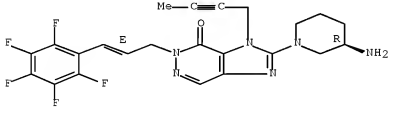
RN 705280-33-7 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[[4-(4-morpholinyl)-2-quinazolinyl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



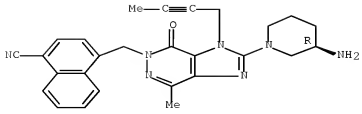
RN 705280-34-8 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(2E)-3-(2,3,4,5,6-pentafluorophenyl)-2-propen-1-yl]- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



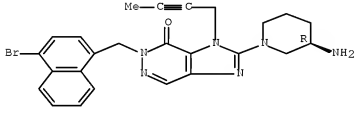
RN 705280-35-9 HCAPLUS
CN 1-Naphthalenecarbonitrile, 4-[[2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,4-dihydro-7-methyl-4-oxo-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.

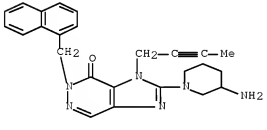


RN 705280-66-6 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-5-[(4-bromo-1-naphthalenyl)methyl]-3-(2-butyn-1-yl)-3,5-dihydro- (CA INDEX NAME)

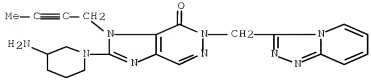
Absolute stereochemistry.



RN 705280-67-7 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3-(2-butyn-1-yl)-3,5-dihydro-5-(1-naphthalenylmethyl)- (CA INDEX NAME)

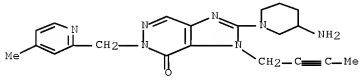


RN 705280-68-8 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3-(2-butyn-1-yl)-3,5-dihydro-5-(1,2,4-triazolo[4,3-a]pyridin-3-ylmethyl)-, hydrochloride (1:1) (CA INDEX NAME)



● HCl

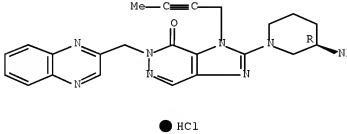
RN 705280-69-9 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3-(2-butyn-1-yl)-3,5-dihydro-5-[(4-methyl-2-pyridinyl)methyl]-, hydrochloride (1:2) (CA INDEX NAME)



●2 HCl

RN 705280-70-2 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-(2-quinoxalinylmethyl)-, hydrochloride (1:1) (CA INDEX NAME)

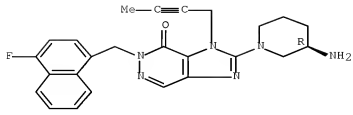
Absolute stereochemistry.



● HCl

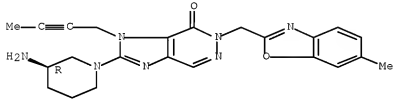
RN 705280-71-3 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-5-[(4-fluoro-1-naphthalenyl)methyl]-3,5-dihydro- (CA INDEX NAME)

Absolute stereochemistry.



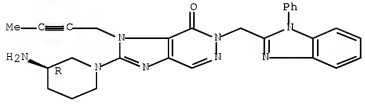
RN 705280-72-4 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(6-methyl-2-benzoxazolyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



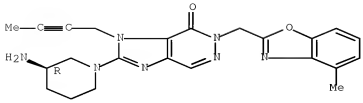
RN 705280-73-5 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(1-phenyl-1H-benzimidazol-2-yl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



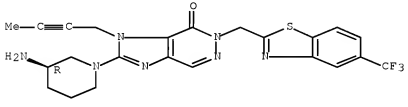
RN 705280-74-6 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(4-methyl-2-benzoxazolyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



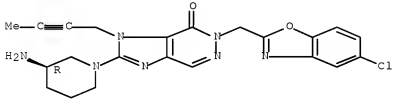
RN 705280-75-7 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[[5-(trifluoromethyl)-2-benzothiazolyl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



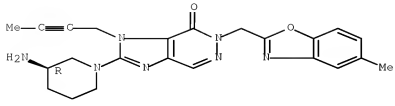
RN 705280-76-8 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-5-[(5-chloro-2-benzoxazolyl)methyl]-3,5-dihydro- (CA INDEX NAME)

Absolute stereochemistry.



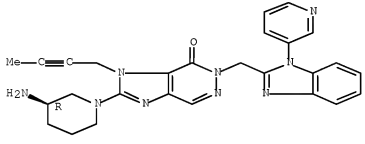
RN 705280-77-9 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[(5-methyl-2-benzoxazolyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



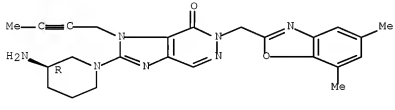
RN 705280-78-0 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,5-dihydro-5-[[1-(3-pyridinyl)-1H-benzimidazol-2-yl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 705280-79-1 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-5-[(5,7-dimethyl-2-benzoxazolyl)methyl]-3,5-dihydro- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:287778 HCAPLUS Full-text
DOCUMENT NUMBER: 140:303701
TITLE: Preparation of piperazine derivatives as dipeptidyl peptidase IV inhibitors
INVENTOR(S): Yasuda, Nobuyuki; Yamazaki, Kazuto
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: PCT Int. Appl., 302 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004028524	A1	20040408	WO 2003-JP12075	20030922
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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AU 2003266559	A1	20040419	AU 2003-266559	20030922
AU 2003266559	A2	20050707		
AU 2003266559	B2	20080124		
EP 1557165	A1	20050727	EP 2003-798438	20030922
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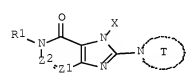
BR 2003014655	A	20050802	BR 2003-14655	20030922
CN 1700911	A	20051123	CN 2003-825394	20030922
NZ 538936	A	20061222	NZ 2003-538936	20030922
US 20060094722	A1	20060504	US 2005-528353	20050317
MX 2005PA03252	A	20050705	MX 2005-PA3252	20050323
NO 2005002018	A	20050622	NO 2005-2018	20050425
IN 2005CN00711	A	20070330	IN 2005-CN711	20050425
PRIORITY APPLN. INFO.:			JP 2002-280137 A	20020926
			JP 2003-117927 A	20030423
			WO 2003-JP12075 W	20030922

OTHER SOURCE(S): MARPAT 140:303701
GI



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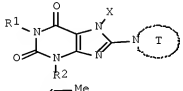

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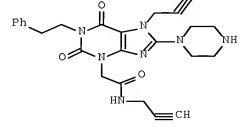


III

AB The title compds. I and II [wherein ring T = (un)substituted heterocyclyl; X = (un)substituted alkyl, alkenyl, alkynyl, aryl, heteroaryl, arylalkyl, or heteroarylalkyl; Z1 and Z2 = independently N or (un)substituted CH; R1 and R2 = independently H, (un)substituted alkyl, etc.] or salts or hydrates thereof are prepared as dipeptidyl peptidase (DPP) IV inhibitors in combination with biguanide. For example, the compound III•HCl was prepared in a multi-step synthesis. III•HCl showed inhibitory activity with IC50 of 0.472 nM against DPP IV in pig. I are useful for the treatment of diabetes, obesity, hyperlipidemia, gastrointestinal disturbance, etc.

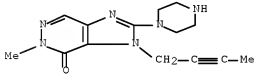
IT 635717-65-6P 635717-66-7P 635717-68-9P
635717-70-3P 635717-75-8P 635717-76-9P
635720-48-8P 635720-64-8P 635720-65-9P
635720-66-0P 635721-30-1P 635721-54-9P
635721-56-1P 635721-60-7P 635722-02-0P
635722-43-9P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of piperazine derivs. as dipeptidyl peptidase IV inhibitors)

RN 635717-65-6 HCAPLUS

CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-methyl-2-(1-piperazinyl)- (CA INDEX NAME)

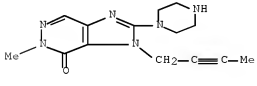


RN 635717-66-7 HCAPLUS

CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-methyl-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635717-65-6
CMF C14 H18 N6 O



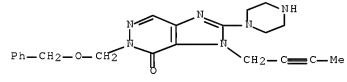
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635717-68-9 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-[(phenylmethoxy)methyl]-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635717-67-8
CMF C21 H24 N6 O2



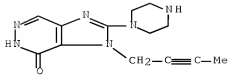
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635717-70-3 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

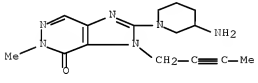
CRN 635717-69-0
CMF C13 H16 N6 O



CM 2

CRN 76-05-1
CMF C2 H F3 O2

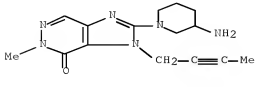
RN 635717-75-8 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3-(2-butyn-1-yl)-3,5-dihydro-5-methyl- (CA INDEX NAME)



RN 635717-76-9 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3-(2-butyn-1-yl)-3,5-dihydro-5-methyl-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635717-75-8
CMF C15 H20 N6 O



CM 2

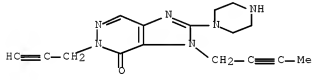
CRN 76-05-1

CMF C2 H F3 O2

RN 635720-48-8 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-2-(1-piperazinyl)-5-(2-propyn-1-yl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635720-47-7
CMF C16 H18 N6 O



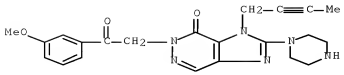
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635720-64-8 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-[2-(3-methoxyphenyl)-2-oxoethyl]-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

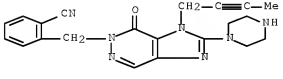
CRN 635720-63-7
CMF C22 H24 N6 O3



CM 2

CRN 76-05-1
CMF C2 H F3 O2

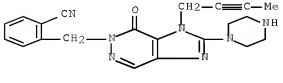
RN 635720-65-9 HCAPLUS
CN Benzonitrile, 2-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]- (CA INDEX NAME)



RN 635720-66-0 HCAPLUS
CN Benzonitrile, 2-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635720-65-9
CMF C21 H21 N7 O



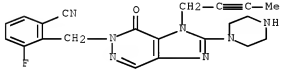
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-30-1 HCAPLUS
CN Benzonitrile, 2-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-3-fluoro-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-29-8
CMF C21 H20 F N7 O



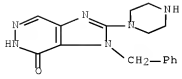
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-54-9 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3,5-dihydro-3-(phenylmethyl)-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-53-8
CMF C16 H18 N6 O



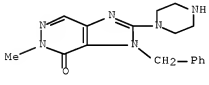
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-56-1 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3,5-dihydro-5-methyl-3-(phenylmethyl)-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-55-0
CMF C17 H20 N6 O



CM 2

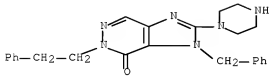
CRN 76-05-1
CMF C2 H F3 O2

RN 635721-60-7 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3,5-dihydro-5-(2-phenylethyl)-3-(phenylmethyl)-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX

NAME)

CM 1

CRN 635721-59-4
CMF C24 H26 N6 O



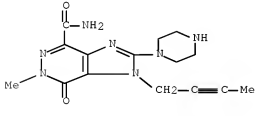
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635722-02-0 HCAPLUS
CN 1H-Imidazo[4,5-d]pyridazine-4-carboxamide, 1-(2-butyn-1-yl)-6,7-dihydro-6-methyl-7-oxo-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635722-01-9
CMF C15 H19 N7 O2



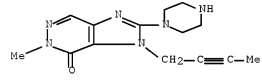
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635722-43-9 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-methyl-2-(1-piperazinyl)-, 4-methylbenzenesulfonate (1:1) (CA INDEX NAME)

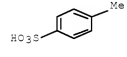
CM 1

CRN 635717-65-6
CMF C14 H18 N6 O

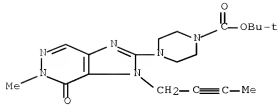


CM 2

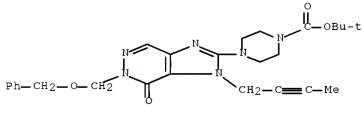
CRN 104-15-4
CMF C7 H8 O3 S



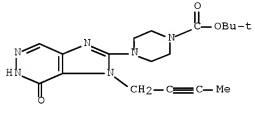
IT 635722-47-3P 635722-78-0P 635723-01-2P
635723-02-3P 635723-03-4P 635723-14-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of piperazine derivs. as dipeptidyl peptidase IV inhibitors)
RN 635722-47-3 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[1-(2-butyn-1-yl)-6,7-dihydro-6-methyl-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



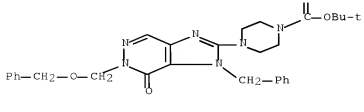
RN 635722-78-0 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[1-(2-butyn-1-yl)-6,7-dihydro-7-oxo-6-[(phenylmethoxy)methyl]-1H-imidazo[4,5-d]pyridazin-2-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



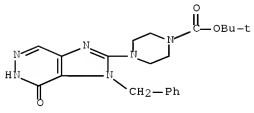
RN 635723-01-2 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[1-(2-butyn-1-yl)-6,7-dihydro-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



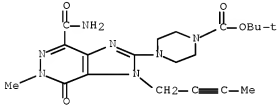
RN 635723-02-3 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[6,7-dihydro-7-oxo-6-[(phenylmethoxy)methyl]-1-(phenylmethyl)-1H-imidazo[4,5-d]pyridazin-2-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



RN 635723-03-4 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[6,7-dihydro-7-oxo-1-(phenylmethyl)-1H-imidazo[4,5-d]pyridazin-2-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



RN 635723-14-7 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[4-(aminocarbonyl)-1-(2-butyn-1-yl)-6,7-dihydro-6-methyl-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



L6 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:991509 HCAPLUS Full-text
DOCUMENT NUMBER: 140:42192
TITLE: Preparation of purinone derivatives as dipeptidylpeptidase IV (DPP-IV) inhibitors
INVENTOR(S): Yoshikawa, Seiji; Emori, Eita; Matsuura, Fumiyoshi; Richard, Clark; Ikuta, Hironori; Kira, Kazunobu; Yasuda, Nobuyuki; Nagakura, Tadashi; Yamazaki, Kazuto
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: PCT Int. Appl., 376 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003104229	A1	20031218	WO 2003-JP7010	20030603
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,				

UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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CA 2485641	A1	20031218	CA 2003-2485641		20030603
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EP 1514552	A1	20050316	EP 2003-733276		20030603
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003011697	A	20050322	BR 2003-11697		20030603
JP 3675813	B2	20050727	JP 2004-511299		20030603
CN 1675208	A	20050928	CN 2003-818968		20030603
TW 273104	B	20070211	TW 2003-92115068		20030603
CN 1931859	A	20070321	CN 2006-10151528		20030603
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MX 2004PA12226	A	20050408	MX 2004-PA12226		20041206
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ZA 2005000041	A	20060601	ZA 2005-41		20050104
NO 2005000054	A	20050210	NO 2005-54		20050105
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US 20060063787	A1	20060323	US 2005-212407		20050826
IN 2006CN03553	A	20070706	IN 2006-CN3553		20060926
PRIORITY APPLN. INFO.:			JP 2002-166069	A	20020606
			JP 2002-209373	A	20020718
			JP 2002-307750	A	20021023
			CN 2003-818968	A3	20030603
			JP 2004-511299	A3	20030603
			WO 2003-JP7010	W	20030603
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			IN 2004-CN2990	A3	20041231

OTHER SOURCE(S): MARPAT 140:42192
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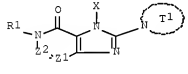

I

AB The title compds. I [wherein T1 is an optionally substituted, monocyclic or bicyclic, 4- to 12-membered, heterocyclic group containing one or two nitrogen atoms in the ring; X is optionally substituted C1-6 alkyl, etc.; Z1 and Z2 each independently is nitrogen, CR2; and R1 and R2 each independently is hydrogen, optionally substituted C1-6 alkyl, optionally substituted C1-6 alkoxy, etc.] are prepared Compds. of this invention in vitro showed IC50 values of 0.001 μM to 1.48 μM against dipeptidylpeptidase IV.

IT 635717-65-6P 635717-66-7P 635717-68-9P
635717-70-3P 635717-76-9P 635717-79-2P
635720-48-8P 635720-50-2P 635720-52-4P
635720-54-6P 635720-56-8P 635720-58-0P

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635720-72-8P 635720-74-0P 635720-76-2P
635720-78-4P 635720-80-8P 635720-82-0P
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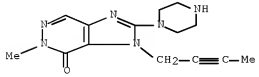
635722-04-2P 635722-06-4P 635722-43-9P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of purinone derivs. as dipeptidylpeptidase IV inhibitors)

RN 635717-65-6 HCAPLUS

CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-methyl-2-(1-piperazinyl)- (CA INDEX NAME)



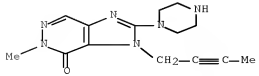
RN 635717-66-7 HCAPLUS

CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-methyl-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635717-65-6

CMF C14 H18 N6 O



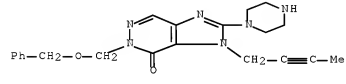
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635717-68-9 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-[(phenylmethoxy)methyl]-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635717-67-8
CMF C21 H24 N6 O2



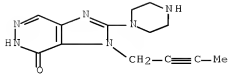
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635717-70-3 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635717-69-0
CMF C13 H16 N6 O



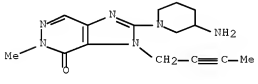
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635717-76-9 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3-(2-butyn-1-yl)-3,5-dihydro-5-methyl-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635717-75-8
CMF C15 H20 N6 O



CM 2

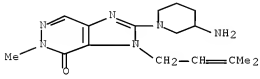
CRN 76-05-1
CMF C2 H F3 O2

RN 635717-79-2 HCAPLUS

CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3,5-dihydro-5-methyl-3-(3-methyl-2-buten-1-yl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635717-78-1
CMF C16 H24 N6 O



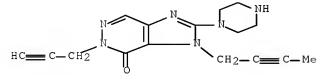
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635720-48-8 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-2-(1-piperazinyl)-5-(2-propyn-1-yl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635720-47-7
CMF C16 H18 N6 O



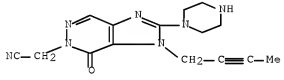
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635720-50-2 HCAPLUS
CN 5H-Imidazo[4,5-d]pyridazine-5-acetonitrile, 3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635720-49-9
CMF C15 H17 N7 O



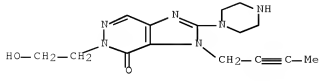
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635720-52-4 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-(2-hydroxyethyl)-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635720-51-3
CMF C15 H20 N6 O2



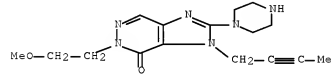
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635720-54-6 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-(2-methoxyethyl)-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635720-53-5
CMF C16 H22 N6 O2



CM 2

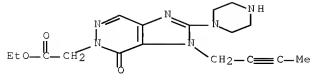
CRN 76-05-1
CMF C2 H F3 O2

RN 635720-56-8 HCAPLUS
CN 5H-Imidazo[4,5-d]pyridazine-5-acetic acid, 3-(2-butynyl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-, ethyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 635720-55-7

CMF C17 H22 N6 O3



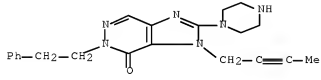
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635720-58-0 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-(2-phenylethyl)-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635720-57-9
CMF C21 H24 N6 O



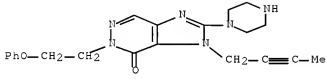
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635720-60-4 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-(2-phenoxyethyl)-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635720-59-1
CMF C21 H24 N6 O2



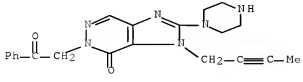
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635720-62-6 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-(2-oxo-2-phenylethyl)-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635720-61-5
CMF C21 H22 N6 O2



CM 2

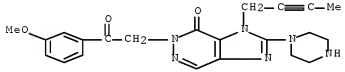
CRN 76-05-1

CMF C2 H F3 O2

RN 635720-64-8 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-[2-(3-methoxyphenyl)-2-oxoethyl]-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635720-63-7
CMF C22 H24 N6 O3



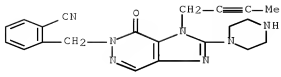
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635720-66-0 HCAPLUS
CN Benzonitrile, 2-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635720-65-9
CMF C21 H21 N7 O



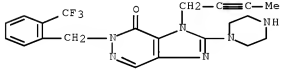
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635720-68-2 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-2-(1-piperazinyl)-5-[[2-(trifluoromethyl)phenyl]methyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635720-67-1
CMF C21 H21 F3 N6 O



CM 2

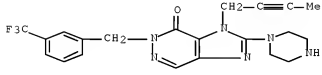
CRN 76-05-1
CMF C2 H F3 O2

RN 635720-70-6 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-2-(1-

piperazinyl)-5-[[3-(trifluoromethyl)phenyl]methyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635720-69-3
CMF C21 H21 F3 N6 O



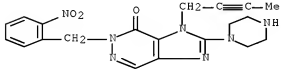
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635720-72-8 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-[(2-nitrophenyl)methyl]-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635720-71-7
CMF C20 H21 N7 O3



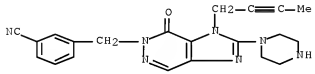
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635720-74-0 HCAPLUS
CN Benzonitrile, 3-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635720-73-9
CMF C21 H21 N7 O



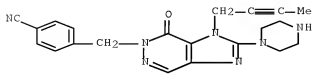
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635720-76-2 HCAPLUS
CN Benzonitrile, 4-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635720-75-1
CMF C21 H21 N7 O



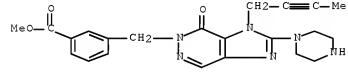
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635720-78-4 HCAPLUS
CN Benzoic acid, 3-[[3-(2-butynyl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-, methyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 635720-77-3
CMF C22 H24 N6 O3



CM 2

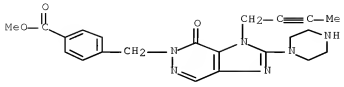
CRN 76-05-1
CMF C2 H F3 O2

RN 635720-80-8 HCAPLUS
CN Benzoic acid, 4-[[3-(2-butynyl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-, methyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 635720-79-5

CMF C22 H24 N6 O3



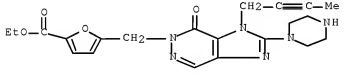
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635720-82-0 HCAPLUS
CN 2-Furancarboxylic acid, 5-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-, ethyl ester, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635720-81-9
CMF C21 H24 N6 O4



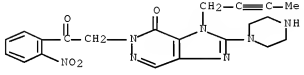
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635720-84-2 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-[2-(2-nitrophenyl)-2-oxoethyl]-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635720-83-1
CMF C21 H21 N7 O4



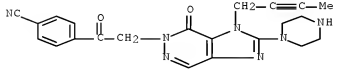
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635720-86-4 HCAPLUS
CN Benzonitrile, 4-[2-[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]acetyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635720-85-3
CMF C22 H21 N7 O2



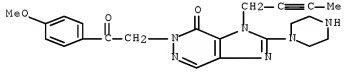
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635720-88-6 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-[2-(4-methoxyphenyl)-2-oxoethyl]-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635720-87-5
CMF C22 H24 N6 O3



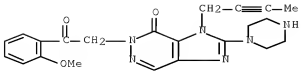
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635720-90-0 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-[2-(2-methoxyphenyl)-2-oxoethyl]-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635720-89-7
CMF C22 H24 N6 O3



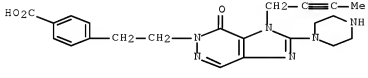
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635720-92-2 HCAPLUS
CN Benzoic acid, 4-[2-[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]ethyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635720-91-1
CMF C22 H24 N6 O3



CM 2

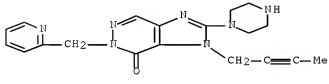
CRN 76-05-1
CMF C2 H F3 O2

RN 635720-94-4 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-2-(1-

piperazinyl)-5-(2-pyridinylmethyl)-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

CM 1

CRN 635720-93-3
CMF C19 H21 N7 O



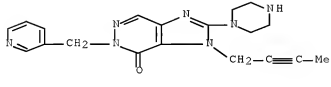
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635720-96-6 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-2-(1-piperazinyl)-5-(3-pyridinylmethyl)-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

CM 1

CRN 635720-95-5
CMF C19 H21 N7 O



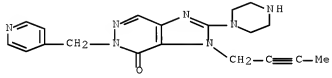
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635720-98-8 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-2-(1-piperazinyl)-5-(4-pyridinylmethyl)-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

CM 1

CRN 635720-97-7
CMF C19 H21 N7 O



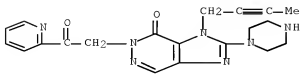
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-00-5 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-[2-oxo-2-(2-pyridinyl)ethyl]-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

CM 1

CRN 635720-99-9
CMF C20 H21 N7 O2



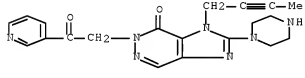
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-02-7 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-[2-oxo-2-(3-pyridinyl)ethyl]-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

CM 1

CRN 635721-01-6
CMF C20 H21 N7 O2



CM 2

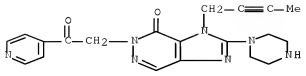
CRN 76-05-1
CMF C2 H F3 O2

RN 635721-04-9 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-[2-oxo-2-(4-pyridinyl)ethyl]-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

CM 1

CRN 635721-03-8

CMF C20 H21 N7 O2



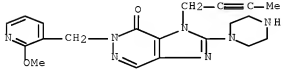
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-06-1 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-[(2-methoxy-3-pyridinyl)methyl]-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-05-0
CMF C20 H23 N7 O2



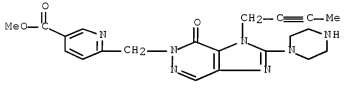
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-08-3 HCAPLUS
CN 3-Pyridinecarboxylic acid, 6-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-, methyl ester, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

CM 1

CRN 635721-07-2
CMF C21 H23 N7 O3



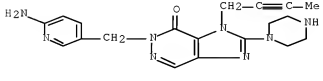
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-10-7 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 5-[(6-amino-3-pyridinyl)methyl]-3-(2-butyn-1-yl)-3,5-dihydro-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-09-4
CMF C19 H22 N8 O



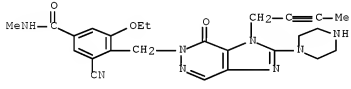
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-12-9 HCAPLUS
CN Benzamide, 4-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-3-cyano-5-ethoxy-N-methyl-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-11-8
CMF C25 H28 N8 O3



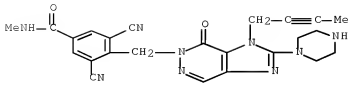
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-14-1 HCAPLUS
CN Benzamide, 4-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-3,5-dicyano-N-methyl-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-13-0
CMF C24 H23 N9 O2



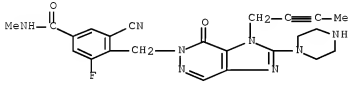
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-16-3 HCAPLUS
CN Benzamide, 4-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-3-cyano-5-fluoro-N-methyl-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-15-2
CMF C23 H23 F N8 O2



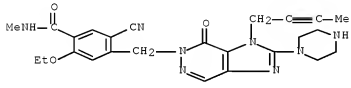
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-18-5 HCAPLUS
CN Benzamide, 4-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-5-cyano-2-ethoxy-N-methyl-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-17-4
CMF C25 H28 N8 O3



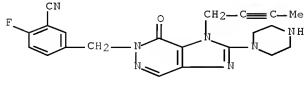
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-21-0 HCAPLUS
CN Benzonitrile, 5-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-2-fluoro-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-20-9
CMF C21 H20 F N7 O



CM 2

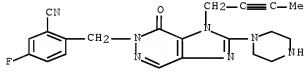
CRN 76-05-1

CMF C2 H F3 O2

RN 635721-24-3 HCAPLUS
CN Benzonitrile, 2-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-5-fluoro-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-23-2
CMF C21 H20 F N7 O



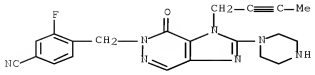
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-27-6 HCAPLUS
CN Benzonitrile, 4-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-3-fluoro-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-26-5
CMF C21 H20 F N7 O



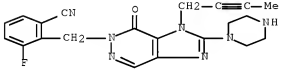
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-30-1 HCAPLUS
CN Benzonitrile, 2-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-3-fluoro-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-29-8
CMF C21 H20 F N7 O



CM 2

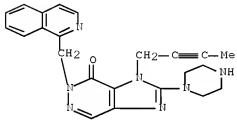
CRN 76-05-1
CMF C2 H F3 O2

RN 635721-32-3 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-(1-

isoquinolinylmethyl)-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-31-2
CMF C23 H23 N7 O



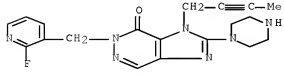
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-34-5 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-5-[(2-fluoro-3-pyridinyl)methyl]-3,5-dihydro-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-33-4
CMF C19 H20 F N7 O



CM 2

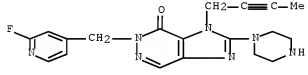
CRN 76-05-1

CMF C2 H F3 O2

RN 635721-36-7 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-5-[(2-fluoro-4-pyridinyl)methyl]-3,5-dihydro-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-35-6
CMF C19 H20 F N7 O



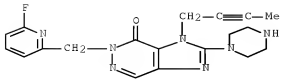
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-38-9 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-5-[(6-fluoro-2-pyridinyl)methyl]-3,5-dihydro-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-37-8
CMF C19 H20 F N7 O



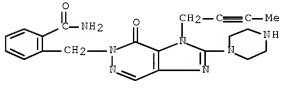
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-41-4 HCAPLUS
CN Benzamide, 2-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-40-3
CMF C21 H23 N7 O2



CM 2

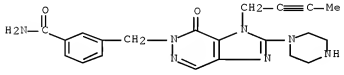
CRN 76-05-1
CMF C2 H F3 O2

RN 635721-44-7 HCAPLUS

CN Benzamide, 3-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-43-6
CMF C21 H23 N7 O2



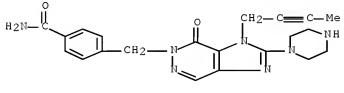
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-46-9 HCAPLUS
CN Benzamide, 4-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-45-8
CMF C21 H23 N7 O2



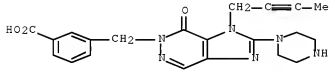
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-48-1 HCAPLUS
CN Benzoic acid, 3-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-47-0
CMF C21 H22 N6 O3



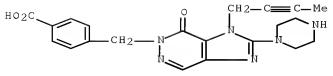
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-50-5 HCAPLUS
CN Benzoic acid, 4-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-49-2
CMF C21 H22 N6 O3



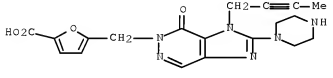
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-52-7 HCAPLUS
CN 2-Furancarboxylic acid, 5-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-51-6
CMF C19 H20 N6 O4



CM 2

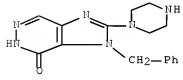
CRN 76-05-1
CMF C2 H F3 O2

RN 635721-54-9 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3,5-dihydro-3-(phenylmethyl)-2-(1-

piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-53-8
CMF C16 H18 N6 O



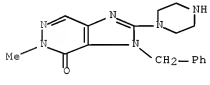
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-56-1 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3,5-dihydro-5-methyl-3-(phenylmethyl)-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-55-0
CMF C17 H20 N6 O



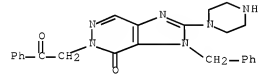
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-58-3 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3,5-dihydro-5-(2-oxo-2-phenylethyl)-3-(phenylmethyl)-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-57-2
CMF C24 H24 N6 O2



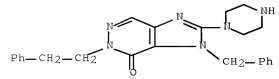
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-60-7 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3,5-dihydro-5-(2-phenylethyl)-3-(phenylmethyl)-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-59-4
CMF C24 H26 N6 O



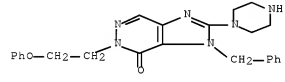
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-62-9 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3,5-dihydro-5-(2-phenoxyethyl)-3-(phenylmethyl)-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-61-8
CMF C24 H26 N6 O2



CM 2

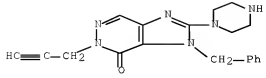
CRN 76-05-1
CMF C2 H F3 O2

RN 635721-64-1 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3,5-dihydro-3-(phenylmethyl)-2-(1-piperazinyl)-5-(2-propyn-1-yl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-63-0

CMF C19 H20 N6 O



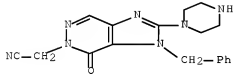
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-66-3 HCAPLUS
CN 5H-Imidazo[4,5-d]pyridazine-5-acetonitrile, 3,4-dihydro-4-oxo-3-(phenylmethyl)-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-65-2
CMF C18 H19 N7 O



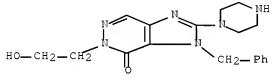
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-68-5 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3,5-dihydro-5-(2-hydroxyethyl)-3-(phenylmethyl)-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-67-4
CMF C18 H22 N6 O2



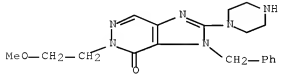
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-70-9 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3,5-dihydro-5-(2-methoxyethyl)-3-(phenylmethyl)-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-69-6
CMF C19 H24 N6 O2



CM 2

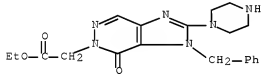
CRN 76-05-1

CMF C2 H F3 O2

RN 635721-72-1 HCAPLUS
CN 5H-Imidazo[4,5-d]pyridazine-5-acetic acid, 3,4-dihydro-4-oxo-3-(phenylmethyl)-2-(1-piperazinyl)-, ethyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 635721-71-0
CMF C20 H24 N6 O3



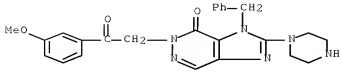
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-74-3 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3,5-dihydro-5-[2-(3-methoxyphenyl)-2-oxoethyl]-3-(phenylmethyl)-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-73-2
CMF C25 H26 N6 O3



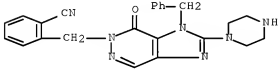
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-76-5 HCAPLUS
CN Benzonitrile, 2-[[3,4-dihydro-4-oxo-3-(phenylmethyl)-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-75-4
CMF C24 H23 N7 O



CM 2

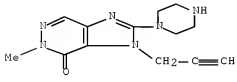
CRN 76-05-1
CMF C2 H F3 O2

RN 635721-78-7 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3,5-dihydro-5-methyl-2-(1-piperazinyl)-3-

(2-propyn-1-yl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-77-6
CMF C13 H16 N6 O



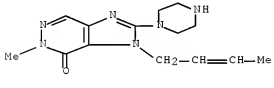
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-80-1 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-buten-1-yl)-3,5-dihydro-5-methyl-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-79-8
CMF C14 H20 N6 O



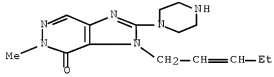
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-82-3 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3,5-dihydro-5-methyl-3-(2-penten-1-yl)-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-81-2
CMF C15 H22 N6 O



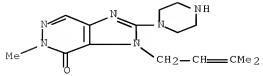
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-84-5 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3,5-dihydro-5-methyl-3-(3-methyl-2-buten-1-yl)-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-83-4
CMF C15 H22 N6 O



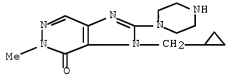
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-86-7 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(cyclopropylmethyl)-3,5-dihydro-5-methyl-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-85-6
CMF C14 H20 N6 O



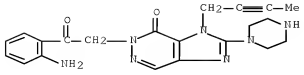
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-88-9 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 5-[2-(2-aminophenyl)-2-oxoethyl]-3-(2-butyn-1-yl)-3,5-dihydro-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

CM 1

CRN 635721-87-8
CMF C21 H23 N7 O2



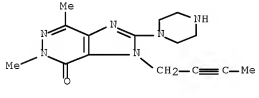
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-90-3 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5,7-dimethyl-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-89-0
CMF C15 H20 N6 O



CM 2

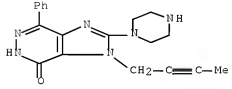
CRN 76-05-1
CMF C2 H F3 O2

RN 635721-92-5 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-7-phenyl-2-

(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-91-4
CMF C19 H20 N6 O



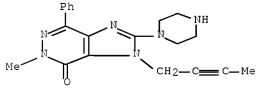
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-94-7 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-methyl-7-phenyl-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-93-6
CMF C20 H22 N6 O



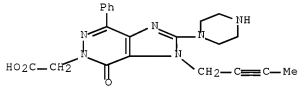
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-96-9 HCAPLUS
CN 5H-Imidazo[4,5-d]pyridazine-5-acetic acid, 3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-7-phenyl-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-95-8
CMF C21 H22 N6 O3



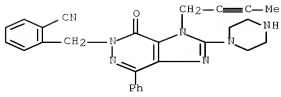
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635721-98-1 HCAPLUS
CN Benzonitrile, 2-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-7-phenyl-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-97-0
CMF C27 H25 N7 O



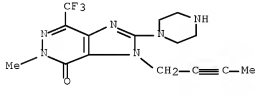
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635722-00-8 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-methyl-2-(1-piperazinyl)-7-(trifluoromethyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635721-99-2
CMF C15 H17 F3 N6 O



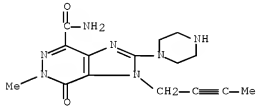
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635722-02-0 HCAPLUS
CN 1H-Imidazo[4,5-d]pyridazine-4-carboxamide, 1-(2-butyn-1-yl)-6,7-dihydro-6-methyl-7-oxo-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635722-01-9
CMF C15 H19 N7 O2



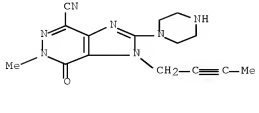
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635722-04-2 HCAPLUS
CN 1H-Imidazo[4,5-d]pyridazine-4-carbonitrile, 1-(2-butyn-1-yl)-6,7-dihydro-6-methyl-7-oxo-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635722-03-1
CMF C15 H17 N7 O



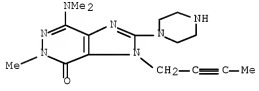
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635722-06-4 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-7-(dimethylamino)-3,5-dihydro-5-methyl-2-(1-piperazinyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 635722-05-3
CMF C16 H23 N7 O



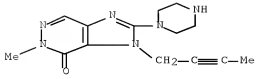
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 635722-43-9 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-methyl-2-(1-piperazinyl)-, 4-methylbenzenesulfonate (1:1) (CA INDEX NAME)

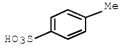
CM 1

CRN 635717-65-6
CMF C14 H18 N6 O

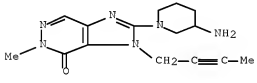


CM 2

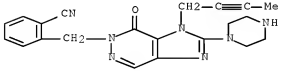
CRN 104-15-4
CMF C7 H8 O3 S



IT 635717-75-8 635720-65-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of purinone derivs. as dipeptidylpeptidase IV inhibitors)
RN 635717-75-8 HCAPLUS
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3-(2-butyn-1-yl)-3,5-dihydro-5-methyl- (CA INDEX NAME)

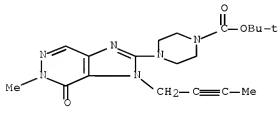


RN 635720-65-9 HCAPLUS
CN Benzonitrile, 2-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]- (CA INDEX NAME)

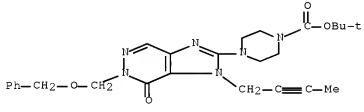


IT 635722-47-3P 635722-78-0P 635723-01-2P
635723-02-3P 635723-03-4P 635723-04-5P
635723-09-0P 635723-14-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of purinone derivs. as dipeptidylpeptidase IV inhibitors)

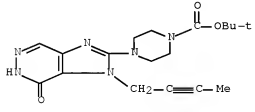
RN 635722-47-3 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[1-(2-butyn-1-yl)-6,7-dihydro-6-methyl-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



RN 635722-78-0 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[1-(2-butyn-1-yl)-6,7-dihydro-7-oxo-6-[(phenylmethoxy)methyl]-1H-imidazo[4,5-d]pyridazin-2-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



RN 635723-01-2 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[1-(2-butyn-1-yl)-6,7-dihydro-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



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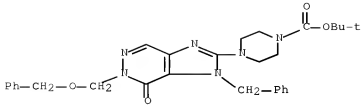
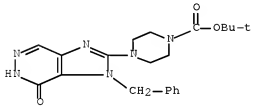
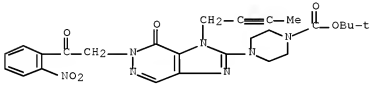


RN 635723-03-4 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[6,7-dihydro-7-oxo-1-(phenylmethyl)-1H-imidazo[4,5-d]pyridazin-2-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



RN 635723-04-5 HCAPLUS
CN 1-Piperazinecarboxylic acid, 4-[1-(2-butyn-1-yl)-6,7-dihydro-6-[2-(2-nitrophenyl)-2-oxoethyl]-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



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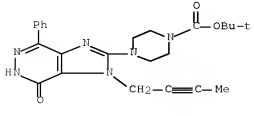

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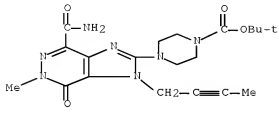
CN 1-Piperazinecarboxylic acid, 4-[4-(aminocarbonyl)-1-(2-butyn-1-yl)-6,7-dihydro-6-methyl-7-oxo-1H-imidazo[4,5-d]pyridazin-2-yl]-, 1,1-dimethylethyl ester (CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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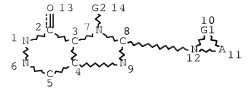

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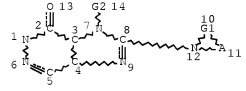

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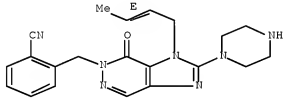
                -7/BI OR 635721-58-3/BI OR 635721-62-9/BI OR 635721-64-1/BI OR
                635721-66-3/BI OR 635721-68-5/BI OR 635721-70-9/BI OR 635721-72
                -1/BI OR 635721-74-3/BI OR 635721-76-5/BI OR 635721-78-7/BI
L8            89 SEA FILE=REGISTRY ABB=ON  PLU=ON  L5 NOT L7


=> => d ide can 18 1 2 3 4 5 6 7 10 11 14 20 25 30 35 40 45 50 55 61 65 70 75 80 87
89

L8   ANSWER 1 OF 89  REGISTRY  COPYRIGHT 2008 ACS on STN
RN   1027933-48-7  REGISTRY
ED   Entered STN:  13 Jun 2008
CN   Benzonitrile, 2-[[3-(2E)-2-buten-1-yl-3,4-dihydro-4-oxo-2-(1-piperazinyl)-
     5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-  (CA INDEX NAME)
FS   STEREOSEARCH
MF   C21 H23 N7 O
SR   Other Sources
       Database: ChemSpider (ChemZoo, Inc.)

Double bond geometry as shown.
```

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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**


L8   ANSWER 2 OF 89  REGISTRY  COPYRIGHT 2008 ACS on STN
RN   1027649-83-7  REGISTRY
ED   Entered STN:  12 Jun 2008
CN   4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3,5-dihydro-5-
     methyl-3-(1-methylpropyl)-  (CA INDEX NAME)
MF   C15 H24 N6 O
SR   Other Sources
       Database: ChemSpider (ChemZoo, Inc.)
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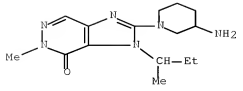
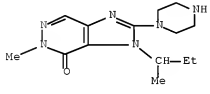


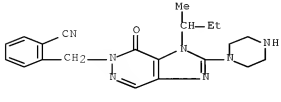
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L8 ANSWER 3 OF 89 REGISTRY COPYRIGHT 2008 ACS on STN
RN 1027225-50-8 REGISTRY
ED Entered STN: 11 Jun 2008
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3,5-dihydro-5-methyl-3-(1-methylpropyl)-2-(1-piperazinyl)- (CA INDEX NAME)
MF C14 H22 N6 O
SR Other Sources
Database: ChemSpider (ChemZoo, Inc.)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

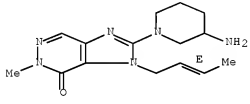
L8 ANSWER 4 OF 89 REGISTRY COPYRIGHT 2008 ACS on STN
RN 1027208-14-5 REGISTRY
ED Entered STN: 11 Jun 2008
CN Benzonitrile, 2-[[3,4-dihydro-3-(1-methylpropyl)-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]- (CA INDEX NAME)
MF C21 H25 N7 O
SR Other Sources
Database: ChemSpider (ChemZoo, Inc.)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

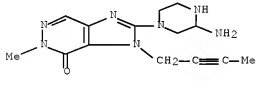
L8 ANSWER 5 OF 89 REGISTRY COPYRIGHT 2008 ACS on STN
RN 1026875-76-2 REGISTRY
ED Entered STN: 10 Jun 2008
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3-(2E)-2-buten-1-yl-3,5-dihydro-5-methyl- (CA INDEX NAME)
FS STEREOSEARCH
MF C15 H22 N6 O
SR Other Sources
Database: ChemSpider (ChemZoo, Inc.)

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

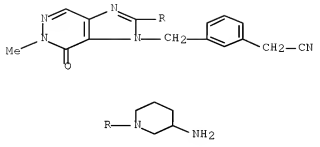
L8 ANSWER 6 OF 89 REGISTRY COPYRIGHT 2008 ACS on STN
RN 1026043-33-3 REGISTRY
ED Entered STN: 06 Jun 2008
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperazinyl)-3-(2-butyn-1-yl)-3,5-dihydro-5-methyl- (CA INDEX NAME)
MF C14 H19 N7 O
SR Other Sources
Database: ChemSpider (ChemZoo, Inc.)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

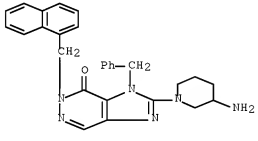
L8 ANSWER 7 OF 89 REGISTRY COPYRIGHT 2008 ACS on STN
RN 919004-37-8 REGISTRY
ED Entered STN: 01 Feb 2007
CN Benzeneacetonitrile, 3-[[2-(3-amino-1-piperidinyl)-6,7-dihydro-6-methyl-7-oxo-1H-imidazo[4,5-d]pyridazin-1-yl]methyl]- (CA INDEX NAME)
MF C20 H23 N7 O
CI COM

SR CA



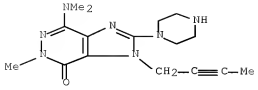
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L8 ANSWER 10 OF 89 REGISTRY COPYRIGHT 2008 ACS on STN
RN 708207-86-7 REGISTRY
ED Entered STN: 11 Jul 2004
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3,5-dihydro-5-(1-naphthalenylmethyl)-3-(phenylmethyl)- (CA INDEX NAME)
MF C28 H28 N6 O
CI COM
SR CA



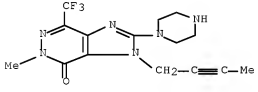
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L8 ANSWER 11 OF 89 REGISTRY COPYRIGHT 2008 ACS on STN
RN 635722-05-3 REGISTRY
ED Entered STN: 09 Jan 2004
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-7-(dimethylamino)-3,5-dihydro-5-methyl-2-(1-piperazinyl)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butynyl)-7-(dimethylamino)-3,5-dihydro-5-methyl-2-(1-piperazinyl)- (9CI)
MF C16 H23 N7 O
CI COM
SR CA



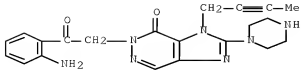
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L8 ANSWER 14 OF 89 REGISTRY COPYRIGHT 2008 ACS on STN
RN 635721-99-2 REGISTRY
ED Entered STN: 09 Jan 2004
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-methyl-2-(1-piperazinyl)-7-(trifluoromethyl)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butynyl)-3,5-dihydro-5-methyl-2-(1-piperazinyl)-7-(trifluoromethyl)- (9CI)
MF C15 H17 F3 N6 O
CI COM
SR CA



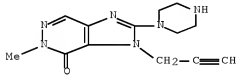
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L8 ANSWER 20 OF 89 REGISTRY COPYRIGHT 2008 ACS on STN
RN 635721-87-8 REGISTRY
ED Entered STN: 09 Jan 2004
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 5-[2-(2-aminophenyl)-2-oxoethyl]-3-(2-butyn-1-yl)-3,5-dihydro-2-(1-piperazinyl)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 5-[2-(2-aminophenyl)-2-oxoethyl]-3-(2-butynyl)-3,5-dihydro-2-(1-piperazinyl)- (9CI)
MF C21 H23 N7 O2
CI COM
SR CA



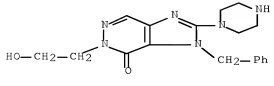
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L8 ANSWER 25 OF 89 REGISTRY COPYRIGHT 2008 ACS on STN
RN 635721-77-6 REGISTRY
ED Entered STN: 09 Jan 2004
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3,5-dihydro-5-methyl-2-(1-piperazinyl)-3-(2-propyn-1-yl)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3,5-dihydro-5-methyl-2-(1-piperazinyl)-3-(2-propynyl)- (9CI)
MF C13 H16 N6 O
CI COM
SR CA



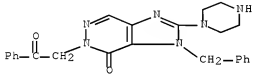
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L8 ANSWER 30 OF 89 REGISTRY COPYRIGHT 2008 ACS on STN
RN 635721-67-4 REGISTRY
ED Entered STN: 09 Jan 2004
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3,5-dihydro-5-(2-hydroxyethyl)-3-(phenylmethyl)-2-(1-piperazinyl)- (CA INDEX NAME)
MF C18 H22 N6 O2
CI COM
SR CA



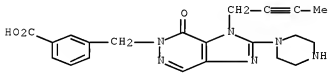
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L8 ANSWER 35 OF 89 REGISTRY COPYRIGHT 2008 ACS on STN
RN 635721-57-2 REGISTRY
ED Entered STN: 09 Jan 2004
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3,5-dihydro-5-(2-oxo-2-phenylethyl)-3-(phenylmethyl)-2-(1-piperazinyl)- (CA INDEX NAME)
MF C24 H24 N6 O2
CI COM
SR CA



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

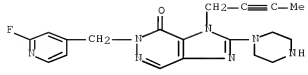
L8 ANSWER 40 OF 89 REGISTRY COPYRIGHT 2008 ACS on STN
RN 635721-47-0 REGISTRY
ED Entered STN: 09 Jan 2004
CN Benzoic acid, 3-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzoic acid, 3-[[3-(2-butynyl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]- (9CI)
MF C21 H22 N6 O3
CI COM
SR CA



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

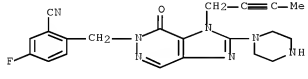
L8 ANSWER 45 OF 89 REGISTRY COPYRIGHT 2008 ACS on STN
RN 635721-35-6 REGISTRY
ED Entered STN: 09 Jan 2004
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-5-[(2-fluoro-4-pyridinyl)methyl]-3,5-dihydro-2-(1-piperazinyl)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butynyl)-5-[(2-fluoro-4-pyridinyl)methyl]-3,5-dihydro-2-(1-piperazinyl)- (9CI)

MF C19 H20 F N7 O
CI COM
SR CA



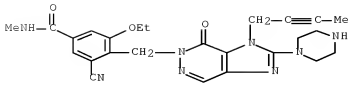
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L8 ANSWER 50 OF 89 REGISTRY COPYRIGHT 2008 ACS on STN
RN 635721-23-2 REGISTRY
ED Entered STN: 09 Jan 2004
CN Benzonitrile, 2-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-5-fluoro- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzonitrile, 2-[[3-(2-butynyl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-5-fluoro- (9CI)
MF C21 H20 F N7 O
CI COM
SR CA



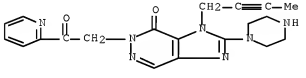
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L8 ANSWER 55 OF 89 REGISTRY COPYRIGHT 2008 ACS on STN
RN 635721-11-8 REGISTRY
ED Entered STN: 09 Jan 2004
CN Benzamide, 4-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-3-cyano-5-ethoxy-N-methyl- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzamide, 4-[[3-(2-butynyl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-3-cyano-5-ethoxy-N-methyl- (9CI)
MF C25 H28 N8 O3
CI COM
SR CA



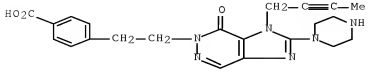
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L8 ANSWER 61 OF 89 REGISTRY COPYRIGHT 2008 ACS on STN
RN 635720-99-9 REGISTRY
ED Entered STN: 09 Jan 2004
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-[2-oxo-2-(2-pyridinyl)ethyl]-2-(1-piperazinyl)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butynyl)-3,5-dihydro-5-[2-oxo-2-(2-pyridinyl)ethyl]-2-(1-piperazinyl)- (9CI)
MF C20 H21 N7 O2
CI COM
SR CA



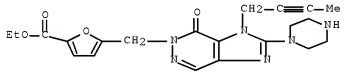
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L8 ANSWER 65 OF 89 REGISTRY COPYRIGHT 2008 ACS on STN
RN 635720-91-1 REGISTRY
ED Entered STN: 09 Jan 2004
CN Benzoic acid, 4-[2-[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]ethyl]- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzoic acid, 4-[2-[3-(2-butynyl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]ethyl]- (9CI)
MF C22 H24 N6 O3
CI COM
SR CA



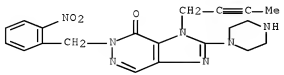
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L8 ANSWER 70 OF 89 REGISTRY COPYRIGHT 2008 ACS on STN
RN 635720-81-9 REGISTRY
ED Entered STN: 09 Jan 2004
CN 2-Furancarboxylic acid, 5-[[3-(2-butyn-1-yl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-, ethyl ester (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2-Furancarboxylic acid, 5-[[3-(2-butynyl)-3,4-dihydro-4-oxo-2-(1-piperazinyl)-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]-, ethyl ester (9CI)
MF C21 H24 N6 O4
CI COM
SR CA



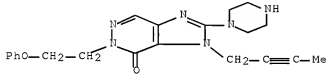
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L8 ANSWER 75 OF 89 REGISTRY COPYRIGHT 2008 ACS on STN
RN 635720-71-7 REGISTRY
ED Entered STN: 09 Jan 2004
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-[(2-nitrophenyl)methyl]-2-(1-piperazinyl)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butynyl)-3,5-dihydro-5-[(2-nitrophenyl)methyl]-2-(1-piperazinyl)- (9CI)
MF C20 H21 N7 O3
CI COM
SR CA



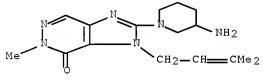
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L8 ANSWER 80 OF 89 REGISTRY COPYRIGHT 2008 ACS on STN
RN 635720-59-1 REGISTRY
ED Entered STN: 09 Jan 2004
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-(2-phenoxyethyl)-2-(1-piperazinyl)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butynyl)-3,5-dihydro-5-(2-phenoxyethyl)-2-(1-piperazinyl)- (9CI)
MF C21 H24 N6 O2
CI COM
SR CA



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L8 ANSWER 87 OF 89 REGISTRY COPYRIGHT 2008 ACS on STN
RN 635717-78-1 REGISTRY
ED Entered STN: 09 Jan 2004
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3,5-dihydro-5-methyl-3-(3-methyl-2-buten-1-yl)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 2-(3-amino-1-piperidinyl)-3,5-dihydro-5-methyl-3-(3-methyl-2-butenyl)- (9CI)
MF C16 H24 N6 O
CI COM
SR CA



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L8 ANSWER 89 OF 89 REGISTRY COPYRIGHT 2008 ACS on STN
RN 635717-67-8 REGISTRY
ED Entered STN: 09 Jan 2004
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butyn-1-yl)-3,5-dihydro-5-[(phenylmethoxy)methyl]-2-(1-piperazinyl)- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 4H-Imidazo[4,5-d]pyridazin-4-one, 3-(2-butynyl)-3,5-dihydro-5-

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MF C21 H24 N6 O2
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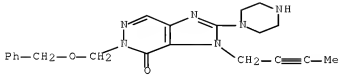
SR CA



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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FILE 'HCAPLUS' ENTERED AT 11:51:52 ON 18 JUN 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 18 Jun 2008 VOL 148 ISS 25
FILE LAST UPDATED: 17 Jun 2008 (20080617/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

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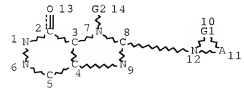

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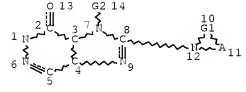

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VAR G2=AK/CY
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L11  ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2005:1005982  HCAPLUS  Full-text
DOCUMENT NUMBER:          143:306327
TITLE:                    Preparation of imidazopyridazinediones as DPP-IV
                          inhibitors
INVENTOR(S):              Eckhardt, Matthias; Himmelsbach, Frank;
                          Kauffmann-Hefner, Iris; Langkopf, Elke; Tadayyon,
                          Mohammad; Thomas, Leo
PATENT ASSIGNEE(S):       Boehringer Ingelheim International G.m.b.H., Germany
SOURCE:                   U.S. Pat. Appl. Publ., 29 pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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US 20050203095	A1	20050915	US 2005-75791		20050309
DE 102004012366	A1	20050929	DE 2004-102004012366		20040313
CA 2559444	A1	20050922	CA 2005-2559444		20050309
WO 2005087774	A1	20050922	WO 2005-EP2524		20050309

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EP 1763530	A1	20070321	EP 2005-728980	20050309

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US 20070142383	A1	20070621	US 2007-676019	20070216

PRIORITY APPLN. INFO.: DE 2004-102004012366A 20040313
US 2004-561321P P 20040412
US 2005-75791 A1 20050309
WO 2005-EP2524 W 20050309

OTHER SOURCE(S): CASREACT 143:306327; MARPAT 143:306327

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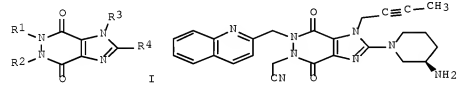


I II

AB Title compds. I [wherein R1 = (hetero)arylmethyl, (hetero)arylcarbonylmethyl; R2 = alkyl, (hetero)aryl; R3 = alkenyl, alkynyl; R4 = piperidin-1-yl; etc., or tautomers, enantiomers, diastereomers and their mixts., and salts thereof], which have valuable pharmacol. properties, particularly an inhibiting effect on the activity of the enzyme dipeptidyl-peptidase-IV (DPP-IV), were prepared For example, II, which showed inhibition against DPP-IV with IC50 of 1 nM, was synthesized in multiple steps. Therefore, I and their pharmaceutical compns. (examples given) are useful for preventing or treating illnesses or conditions connected with an increased DPP-IV activity or capable of being prevented or alleviated by reducing the DPP-IV activity, particularly type I or type II diabetes mellitus.

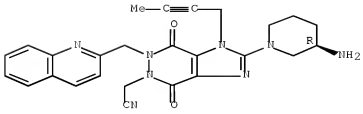
IT 864673-50-7P, (R)-1-(But-2-ynyl)-2-(3-aminopiperidin-1-yl)-5-cyanomethyl-6-(quinolin-2-ylmethyl)-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-51-8P 864673-52-9P, (R)-1-(But-2-ynyl)-2-(3-aminopiperidin-1-yl)-5-methyl-6-(quinolin-2-ylmethyl)-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-53-0P 864673-54-1P, (R)-1-(But-2-ynyl)-2-(3-aminopiperidin-1-yl)-5-(prop-2-enyl)-6-(quinolin-2-ylmethyl)-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-55-2P 864673-56-3P, (R)-1-(But-2-ynyl)-2-(3-aminopiperidin-1-yl)-5-

(phenylmethyl)-6-(quinolin-2-ylmethyl)-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-57-4P 864673-58-5P, (R)-1-(But-2-ynyl)-2-(3-aminopiperidin-1-yl)-5-methyl-6-(naphth-1-ylmethyl)-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-59-6P 864673-61-0P 864673-62-1P, (R)-1-(But-2-ynyl)-2-(3-aminopiperidin-1-yl)-5-[(aminocarbonyl)methyl]-6-[(quinolin-2-yl)methyl]-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-63-2P, (R)-1-(But-2-ynyl)-2-(3-aminopiperidin-1-yl)-5-[(pyridin-3-yl)methyl]-6-[(quinolin-2-yl)methyl]-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-64-3P, (R)-1-(But-2-ynyl)-2-(3-aminopiperidin-1-yl)-5-(prop-2-ynyl)-6-[(quinolin-2-yl)methyl]-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-66-5P 864673-67-6P, (R)-1-(But-2-ynyl)-2-(3-aminopiperidin-1-yl)-5-methyl-6-(3-methylisoquinolin-1-ylmethyl)-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-68-7P 864673-69-8P, (R)-1-(But-2-ynyl)-2-(3-aminopiperidin-1-yl)-5-methyl-6-(phenylcarbonylmethyl)-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-70-1P 864673-71-2P, (R)-1-(But-2-ynyl)-2-(3-aminopiperidin-1-yl)-5-methyl-6-[(4-methylquinazolin-2-yl)methyl]-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-72-3P, (R)-1-(But-2-ynyl)-2-(3-aminopiperidin-1-yl)-5-methyl-6-(2-cyanobenzyl)-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-73-4P, (R)-1-(But-2-ynyl)-2-(3-aminopiperidin-1-yl)-5-(2-fluoroethyl)-6-(4-methylquinazolin-2-ylmethyl)-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-74-5P 864673-75-6P, 1-(But-2-ynyl)-2-(piperazin-1-yl)-5-methyl-6-(quinolin-4-ylmethyl)-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-76-7P, 1-(But-2-ynyl)-2-(piperazin-1-yl)-5-methyl-6-(quinolin-2-ylmethyl)-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-77-8P, (R)-1-(But-2-ynyl)-2-(3-aminopiperidin-1-yl)-5-[[hydroxycarbonyl]methyl]-6-(naphth-1-ylmethyl)-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-78-9P, (R)-1-(But-2-ynyl)-2-(3-aminopiperidin-1-yl)-5-[[aminocarbonyl]methyl]-6-(naphth-1-ylmethyl)-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-79-0P, (R)-1-(But-2-ynyl)-2-(3-aminopiperidin-1-yl)-5-(pyridin-3-ylmethyl)-6-(naphth-1-ylmethyl)-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-80-3P, (R)-1-(But-2-ynyl)-2-(3-aminopiperidin-1-yl)-5-(prop-2-ynyl)-6-(naphth-1-ylmethyl)-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-81-4P, (R)-1-(But-2-ynyl)-2-(3-aminopiperidin-1-yl)-5-(pyridin-4-ylmethyl)-6-(naphth-1-ylmethyl)-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibitor; preparation of imidazopyridazinediones as DPP-IV inhibitors)

RN 864673-50-7 HCAPLUS

CN 5H-Imidazo[4,5-d]pyridazine-5-acetonitrile, 2-[(3R)-3-amino-1-piperidinyl]-1-(2-butyn-1-yl)-1,4,6,7-tetrahydro-4,7-dioxo-6-(2-quinolinylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 864673-51-8 HCAPLUS
CN 5H-Imidazo[4,5-d]pyridazine-5-acetonitrile, 2-[(3R)-3-amino-1-piperidinyl]-1-(2-butyn-1-yl)-1,4,6,7-tetrahydro-4,7-dioxo-6-(2-quinolinylmethyl)-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

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CRN 864673-50-7
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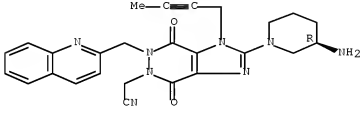
Absolute stereochemistry.

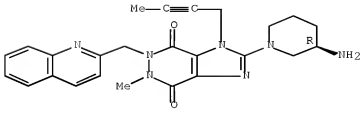


CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 864673-52-9 HCAPLUS
CN 1H-Imidazo[4,5-d]pyridazine-4,7-dione, 2-[(3R)-3-amino-1-piperidinyl]-1-(2-butyn-1-yl)-5,6-dihydro-5-methyl-6-(2-quinolinylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.



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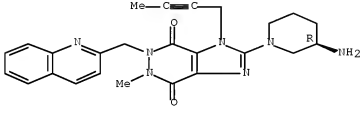
CN 1H-Imidazo[4,5-d]pyridazine-4,7-dione, 2-[(3R)-3-amino-1-piperidinyl]-1-(2-butyn-1-yl)-5,6-dihydro-5-methyl-6-(2-quinolinylmethyl)-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

CM 1

CRN 864673-52-9
CMF C25 H27 N7 O2

Absolute stereochemistry.

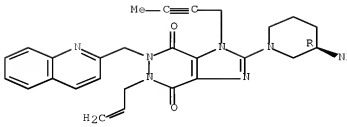


CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 864673-54-1 HCAPLUS
CN 1H-Imidazo[4,5-d]pyridazine-4,7-dione, 2-[(3R)-3-amino-1-piperidinyl]-1-(2-butyn-1-yl)-5,6-dihydro-5-(2-propen-1-yl)-6-(2-quinolinylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.



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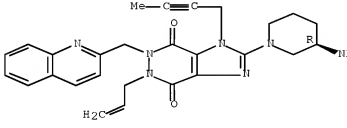
CM 1

CRN 864673-54-1
CMF C27 H29 N7 O2

Absolute stereochemistry.

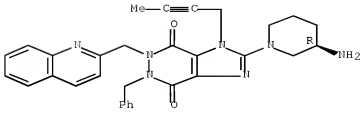


CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 864673-56-3 HCAPLUS
CN 1H-Imidazo[4,5-d]pyridazine-4,7-dione, 2-[(3R)-3-amino-1-piperidinyl]-1-(2-butyn-1-yl)-5,6-dihydro-5-(phenylmethyl)-6-(2-quinolinylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.

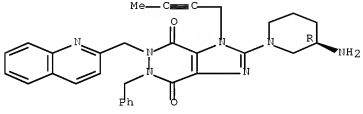


RN 864673-57-4 HCAPLUS
CN 1H-Imidazo[4,5-d]pyridazine-4,7-dione, 2-[(3R)-3-amino-1-piperidinyl]-1-(2-butyn-1-yl)-5,6-dihydro-5-(phenylmethyl)-6-(2-quinolinylmethyl)-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

CM 1

CRN 864673-56-3
CMF C31 H31 N7 O2

Absolute stereochemistry.

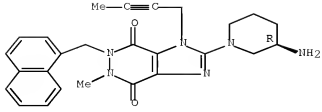


CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 864673-58-5 HCAPLUS
CN 1H-Imidazo[4,5-d]pyridazine-4,7-dione, 2-[(3R)-3-amino-1-piperidinyl]-1-(2-butyn-1-yl)-5,6-dihydro-5-methyl-6-(1-naphthalenylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.



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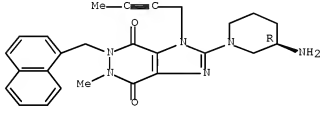
CN 1H-Imidazo[4,5-d]pyridazine-4,7-dione, 2-[(3R)-3-amino-1-piperidinyl]-1-(2-butyn-1-yl)-5,6-dihydro-5-methyl-6-(1-naphthalenylmethyl)-, 2,2,2-trifluoroacetate (1:1) (CA INDEX NAME)

CM 1

CRN 864673-58-5
CMF C26 H28 N6 O2

Absolute stereochemistry.



CM 2

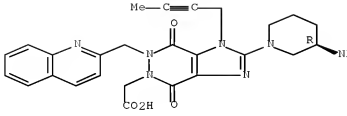
CRN 76-05-1
CMF C2 H F3 O2

RN 864673-61-0 HCAPLUS
CN 5H-Imidazo[4,5-d]pyridazine-5-acetic acid, 2-[(3R)-3-amino-1-piperidinyl]-1-(2-butyn-1-yl)-1,4,6,7-tetrahydro-4,7-dioxo-6-(2-quinolinylmethyl)-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

CM 1

CRN 864673-60-9
CMF C26 H27 N7 O4

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 864673-62-1 HCAPLUS
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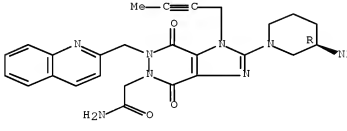
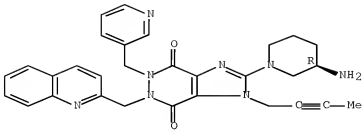
Absolute stereochemistry.



RN 864673-63-2 HCAPLUS
CN 1H-Imidazo[4,5-d]pyridazine-4,7-dione, 2-[(3R)-3-amino-1-piperidinyl]-1-(2-butyn-1-yl)-5,6-dihydro-5-(3-pyridinylmethyl)-6-(2-quinolinylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.



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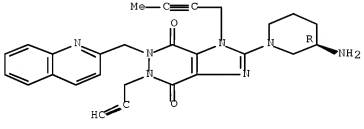
Absolute stereochemistry.



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CRN 864673-65-4
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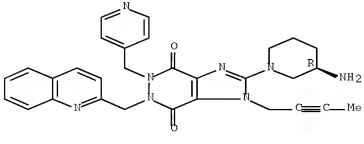
Absolute stereochemistry.

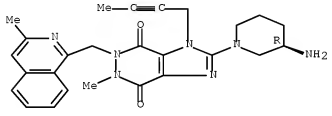


CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 864673-67-6 HCAPLUS
CN 1H-Imidazo[4,5-d]pyridazine-4,7-dione, 2-[(3R)-3-amino-1-piperidinyl]-1-(2-butyn-1-yl)-5,6-dihydro-5-methyl-6-[(3-methyl-1-isoquinolinyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.

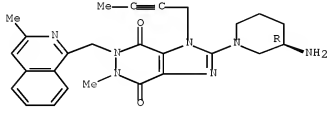


RN 864673-68-7 HCAPLUS
CN 1H-Imidazo[4,5-d]pyridazine-4,7-dione, 2-[(3R)-3-amino-1-piperidinyl]-1-(2-butyn-1-yl)-5,6-dihydro-5-methyl-6-[(3-methyl-1-isoquinolinyl)methyl]-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 864673-67-6
CMF C26 H29 N7 O2

Absolute stereochemistry.

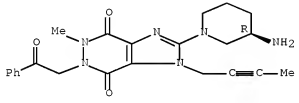


CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 864673-69-8 HCAPLUS
CN 1H-Imidazo[4,5-d]pyridazine-4,7-dione, 2-[(3R)-3-amino-1-piperidinyl]-1-(2-butyn-1-yl)-5,6-dihydro-5-methyl-6-(2-oxo-2-phenylethyl)- (CA INDEX NAME)

Absolute stereochemistry.

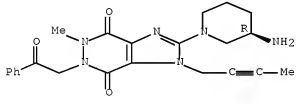


RN 864673-70-1 HCAPLUS
CN 1H-Imidazo[4,5-d]pyridazine-4,7-dione, 2-[(3R)-3-amino-1-piperidinyl]-1-(2-butyn-1-yl)-5,6-dihydro-5-methyl-6-(2-oxo-2-phenylethyl)-, 2,2,2-trifluoroacetate (1:?) (CA INDEX NAME)

CM 1

CRN 864673-69-8
CMF C23 H26 N6 O3

Absolute stereochemistry.

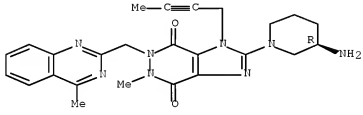


CM 2

CRN 76-05-1
CMF C2 H F3 O2

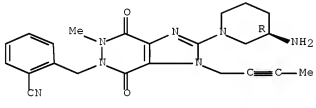
RN 864673-71-2 HCAPLUS
CN 1H-Imidazo[4,5-d]pyridazine-4,7-dione, 2-[(3R)-3-amino-1-piperidinyl]-1-(2-butyn-1-yl)-5,6-dihydro-5-methyl-6-[(4-methyl-2-quinazolinyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.



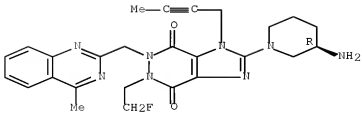
RN 864673-72-3 HCAPLUS
CN Benzonitrile, 2-[[2-[(3R)-3-amino-1-piperidinyl]-3-(2-butyn-1-yl)-3,4,6,7-tetrahydro-6-methyl-4,7-dioxo-5H-imidazo[4,5-d]pyridazin-5-yl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



RN 864673-73-4 HCAPLUS
CN 1H-Imidazo[4,5-d]pyridazine-4,7-dione, 2-[(3R)-3-amino-1-piperidinyl]-1-(2-butyn-1-yl)-5-(2-fluoroethyl)-5,6-dihydro-6-[(4-methyl-2-quinazolinyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.

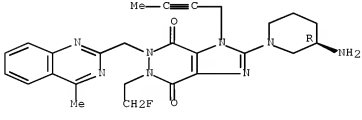


RN 864673-74-5 HCAPLUS
CN 1H-Imidazo[4,5-d]pyridazine-4,7-dione, 2-[(3R)-3-amino-1-piperidinyl]-1-(2-butyn-1-yl)-5-(2-fluoroethyl)-5,6-dihydro-6-[(4-methyl-2-quinazolinyl)methyl]-, 2,2,2-trifluoroacetate (1:2) (CA INDEX NAME)

CM 1

CRN 864673-73-4
CMF C26 H29 F N8 O2

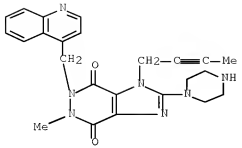
Absolute stereochemistry.



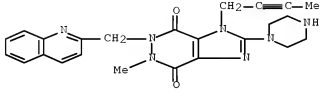
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 864673-75-6 HCAPLUS
CN 1H-Imidazo[4,5-d]pyridazine-4,7-dione, 1-(2-butyn-1-yl)-5,6-dihydro-5-methyl-2-(1-piperazinyl)-6-(4-quinolinylmethyl)- (CA INDEX NAME)

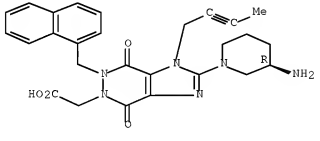


RN 864673-76-7 HCAPLUS
CN 1H-Imidazo[4,5-d]pyridazine-4,7-dione, 1-(2-butyn-1-yl)-5,6-dihydro-5-methyl-2-(1-piperazinyl)-6-(2-quinolinylmethyl)- (CA INDEX NAME)



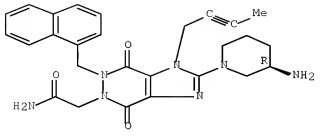
RN 864673-77-8 HCAPLUS
CN 5H-Imidazo[4,5-d]pyridazine-5-acetic acid, 2-[(3R)-3-amino-1-piperidinyl]-1-(2-butyn-1-yl)-1,4,6,7-tetrahydro-6-(1-naphthalenylmethyl)-4,7-dioxo- (CA INDEX NAME)

Absolute stereochemistry.



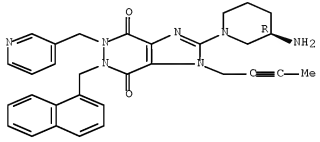
RN 864673-78-9 HCAPLUS
CN 5H-Imidazo[4,5-d]pyridazine-5-acetamide, 2-[(3R)-3-amino-1-piperidinyl]-1-(2-butyn-1-yl)-1,4,6,7-tetrahydro-6-(1-naphthalenylmethyl)-4,7-dioxo- (CA INDEX NAME)

Absolute stereochemistry.



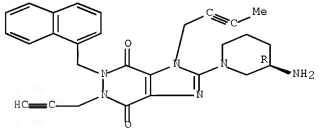
RN 864673-79-0 HCAPLUS
CN 1H-Imidazo[4,5-d]pyridazine-4,7-dione, 2-[(3R)-3-amino-1-piperidinyl]-1-(2-butyn-1-yl)-5,6-dihydro-6-(1-naphthalenylmethyl)-5-(3-pyridinylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.



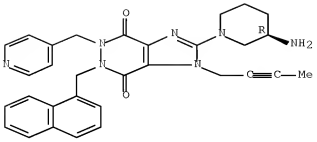
RN 864673-80-3 HCAPLUS
CN 1H-Imidazo[4,5-d]pyridazine-4,7-dione, 2-[(3R)-3-amino-1-piperidinyl]-1-(2-butyn-1-yl)-5,6-dihydro-6-(1-naphthalenylmethyl)-5-(2-propyn-1-yl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 864673-81-4 HCAPLUS
CN 1H-Imidazo[4,5-d]pyridazine-4,7-dione, 2-[(3R)-3-amino-1-piperidinyl]-1-(2-butyn-1-yl)-5,6-dihydro-6-(1-naphthalenylmethyl)-5-(4-pyridinylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.

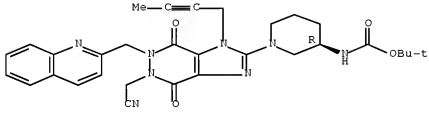


IT 864673-31-4P, (R)-1-(But-2-ynyl)-2-[3-[(tert-butoxycarbonyl)amino]piperidin-1-yl]-5-cyanomethyl-6-[(quinolin-2-yl)methyl]-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-32-5P, (R)-1-(But-2-ynyl)-2-[3-[(tert-butoxycarbonyl)amino]piperidin-1-yl]-5-methyl-6-[(quinolin-2-yl)methyl]-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-33-6P, (R)-1-(But-2-ynyl)-2-[3-[(tert-butoxycarbonyl)amino]piperidin-1-yl]-5-(prop-2-enyl)-6-[(quinolin-2-yl)methyl]-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-34-7P, (R)-1-(But-2-ynyl)-2-[3-[(tert-butoxycarbonyl)amino]piperidin-1-yl]-5-(phenylmethyl)-6-[(quinolin-2-yl)methyl]-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-35-8P, (R)-1-(But-2-ynyl)-2-[3-[(tert-butoxycarbonyl)amino]piperidin-1-yl]-5-methyl-6-[(naphth-1-yl)methyl]-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-36-9P, (R)-1-(But-2-ynyl)-2-[3-[(tert-butoxycarbonyl)amino]piperidin-1-yl]-5-[(tert-butoxycarbonyl)methyl]-6-[(quinolin-2-yl)methyl]-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-37-0P, (R)-1-(But-2-ynyl)-2-[3-[(tert-butoxycarbonyl)amino]piperidin-1-yl]-5-[(aminocarbonyl)methyl]-6-[(quinolin-2-yl)methyl]-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-38-1P, (R)-1-(But-2-ynyl)-2-[3-[(tert-butoxycarbonyl)amino]piperidin-1-yl]-5-[(pyridin-3-yl)methyl]-6-[(quinolin-2-yl)methyl]-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-39-2P, (R)-1-(But-2-ynyl)-2-[3-[(tert-butoxycarbonyl)amino]piperidin-1-yl]-5-(prop-2-ynyl)-6-[(quinolin-2-yl)methyl]-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-40-5P, (R)-1-(But-2-ynyl)-2-[3-[(tert-butoxycarbonyl)amino]piperidin-1-yl]-5-[(pyridin-4-yl)methyl]-6-[(quinolin-2-yl)methyl]-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-41-6P, (R)-1-(But-2-ynyl)-2-[3-[(tert-butoxycarbonyl)amino]piperidin-1-yl]-5-methyl-6-(2-phenylsulfonylethyl)-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-42-7P, (R)-1-(But-2-ynyl)-2-[3-[(tert-butoxycarbonyl)amino]piperidin-1-yl]-5-(2-fluoroethyl)-6-(2-phenylsulfonylethyl)-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-43-8P, (R)-1-(But-2-ynyl)-2-[3-[(tert-butoxycarbonyl)amino]piperidin-1-yl]-5-methyl-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-44-9P, (R)-1-(But-2-ynyl)-2-[3-[(tert-butoxycarbonyl)amino]piperidin-1-yl]-5-(2-fluoroethyl)-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-45-0P, (R)-1-(But-2-ynyl)-2-[3-[(tert-butoxycarbonyl)amino]piperidin-1-yl]-5-methyl-6-[(3-methylisoquinolin-1-yl)methyl]-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-46-1P, (R)-1-(But-2-ynyl)-2-[3-[(tert-butoxycarbonyl)amino]piperidin-1-yl]-5-methyl-6-[(phenylcarbonyl)methyl]-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-47-2P, (R)-1-(But-2-ynyl)-2-[3-[(tert-butoxycarbonyl)amino]piperidin-1-yl]-5-

methyl-6-[(4-methylquinazolin-2-yl)methyl]-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-48-2P, (R)-1-(But-2-ynyl)-2-[3-[(tert-butoxycarbonyl)amino]piperidin-1-yl]-5-methyl-6-(2-cyanobenzyl)-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione 864673-49-3P, (R)-1-(But-2-ynyl)-2-[3-[(tert-butoxycarbonyl)amino]piperidin-1-yl]-5-(2-fluoroethyl)-6-[(4-methylquinazolin-2-yl)methyl]-5,6-dihydro-1H-imidazo[4,5-d]pyridazine-4,7-dione
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of imidazopyridazinediones as DPP-IV inhibitors)

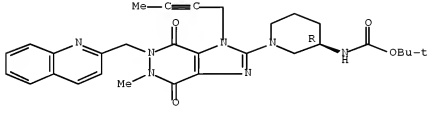
RN 864673-31-4 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-5-(cyanomethyl)-4,5,6,7-tetrahydro-4,7-dioxo-6-(2-quinolinylmethyl)-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



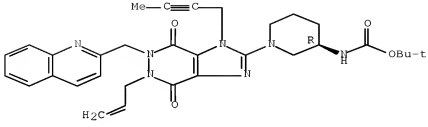
RN 864673-32-5 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-4,5,6,7-tetrahydro-5-methyl-4,7-dioxo-6-(2-quinolinylmethyl)-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



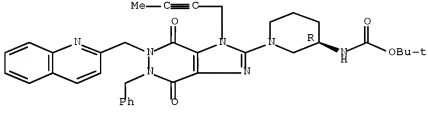
RN 864673-33-6 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-4,5,6,7-tetrahydro-4,7-dioxo-5-(2-propenyl)-6-(2-quinolinylmethyl)-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



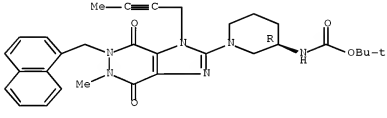
RN 864673-34-7 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-4,5,6,7-tetrahydro-4,7-dioxo-5-(phenylmethyl)-6-(2-quinolinylmethyl)-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



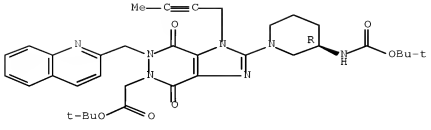
RN 864673-35-8 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-4,5,6,7-tetrahydro-5-methyl-6-(1-naphthalenylmethyl)-4,7-dioxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



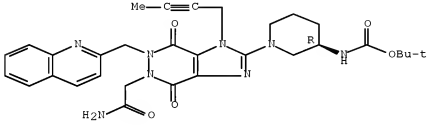
RN 864673-36-9 HCAPLUS
CN 5H-Imidazo[4,5-d]pyridazine-5-acetic acid, 1-(2-butyn-1-yl)-2-[(3R)-3-[[(1,1-dimethylethoxy)carbonyl]amino]-1-piperidinyl]-1,4,6,7-tetrahydro-4,7-dioxo-6-(2-quinolinylmethyl)-, 1,1-dimethylethyl ester (CA INDEX NAME)

Absolute stereochemistry.



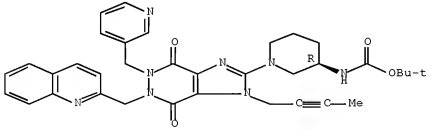
RN 864673-37-0 HCAPLUS
CN Carbamic acid, [(3R)-1-[5-(2-amino-2-oxoethyl)-1-(2-butynyl)-4,5,6,7-tetrahydro-4,7-dioxo-6-(2-quinolinylmethyl)-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



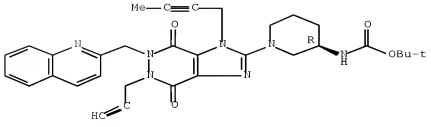
RN 864673-38-1 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-4,5,6,7-tetrahydro-4,7-dioxo-5-(3-pyridinylmethyl)-6-(2-quinolinylmethyl)-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



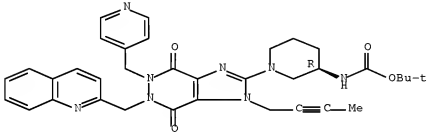
RN 864673-39-2 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-4,5,6,7-tetrahydro-4,7-dioxo-5-(2-propynyl)-6-(2-quinolinylmethyl)-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



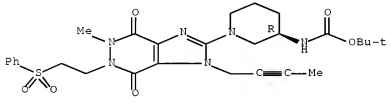
RN 864673-40-5 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-4,5,6,7-tetrahydro-4,7-dioxo-5-(4-pyridinylmethyl)-6-(2-quinolinylmethyl)-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



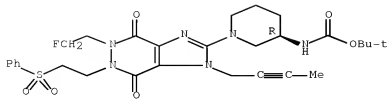
RN 864673-41-6 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-4,5,6,7-tetrahydro-5-methyl-4,7-dioxo-6-[2-(phenylsulfonyl)ethyl]-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



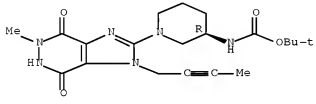
RN 864673-42-7 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-5-(2-fluoroethyl)-4,5,6,7-tetrahydro-4,7-dioxo-6-[2-(phenylsulfonyl)ethyl]-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



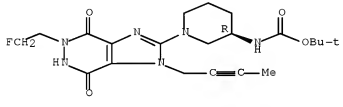
RN 864673-43-8 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-4,5,6,7-tetrahydro-5-methyl-4,7-dioxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



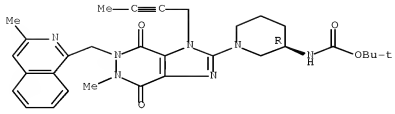
RN 864673-44-9 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-5-(2-fluoroethyl)-4,5,6,7-tetrahydro-4,7-dioxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



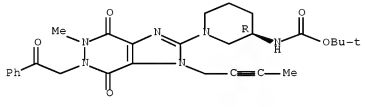
RN 864673-45-0 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-4,5,6,7-tetrahydro-5-methyl-6-[(3-methyl-1-isoquinolinyl)methyl]-4,7-dioxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



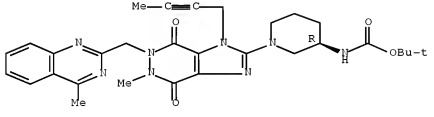
RN 864673-46-1 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-4,5,6,7-tetrahydro-5-methyl-4,7-dioxo-6-(2-oxo-2-phenylethyl)-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



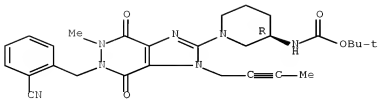
RN 864673-47-2 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-4,5,6,7-tetrahydro-5-methyl-6-[(4-methyl-2-quinazolinyl)methyl]-4,7-dioxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



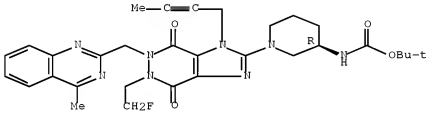
RN 864673-48-3 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-6-[(2-cyanophenyl)methyl]-4,5,6,7-tetrahydro-5-methyl-4,7-dioxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 864673-49-4 HCAPLUS
CN Carbamic acid, [(3R)-1-[1-(2-butynyl)-5-(2-fluoroethyl)-4,5,6,7-tetrahydro-6-[(4-methyl-2-quinazolinyl)methyl]-4,7-dioxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:1080909 HCAPLUS Full-text
DOCUMENT NUMBER: 142:56329
TITLE: Preparation of 1H-imidazo[4,5-d]pyridazines as DPP-IV inhibitors for the treatment of NIDDM
INVENTOR(S): Kuroda, Akio; Sawada, Yuki; Wada, Aiko
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004108730	A1	20041216	WO 2004-JP7996	20040602

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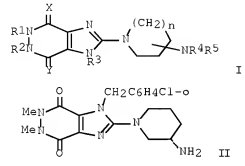
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: AU 2003-902828 A 20030605
OTHER SOURCE(S): CASREACT 142:56329; MARPAT 142:56329
GI



I

II

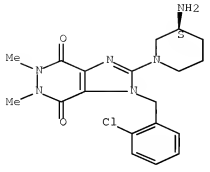
AB The title compds. I [X and Y independently = O, S, substituted imino; R1 and R2 independently = H or (lower)alkyl; R3 = (lower)alkenyl, etc.; R4 and R5 independently = H or (lower)alkyl; n = 0, 1, 2, 3 or 4] were prepared to inhibit DPP-IV activity. They are therefore useful in the treatment of conditions mediated by DPP-IV, such as NIDDM. Thus, 2-bromo-1-(2-chlorobenzyl)-1H-imidazole-4,5-dicarboxylic acid, prepd from di-Me 1H-imidazole-4,5-dicarboxylate, was cyclized with 1,2-dimethylhydrazine dihydrochloride followed by reaction with tert-Bu (S)-3- piperidinecarbamate and then hydrolysis to give the 1H-imidazo[4,5- d]pyridazine deriv II.

IT 808736-66-5P 808736-71-2P 808736-76-7P
808736-78-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of 1H-imidazo[4,5-d]pyridazines as DPP-IV inhibitors for treatment of NIDDM)

RN 808736-66-5 HCAPLUS

CN 1H-Imidazo[4,5-d]pyridazine-4,7-dione, 2-[(3S)-3-amino-1-piperidinyl]-1-[(2-chlorophenyl)methyl]-5,6-dihydro-5,6-dimethyl-, hydrochloride (1:2) (CA INDEX NAME)

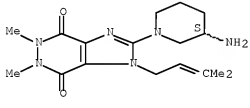
Absolute stereochemistry.



●2 HCl

RN 808736-71-2 HCAPLUS
CN 1H-Imidazo[4,5-d]pyridazine-4,7-dione, 2-[(3S)-3-amino-1-piperidinyl]-5,6-dihydro-5,6-dimethyl-1-(3-methyl-2-buten-1-yl)-, hydrochloride (1:2) (CA INDEX NAME)

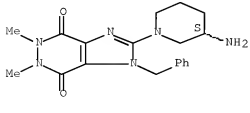
Absolute stereochemistry.



●2 HCl

RN 808736-76-7 HCAPLUS
CN 1H-Imidazo[4,5-d]pyridazine-4,7-dione, 2-[(3S)-3-amino-1-piperidinyl]-5,6-dihydro-5,6-dimethyl-1-(phenylmethyl)-, hydrochloride (1:2) (CA INDEX NAME)

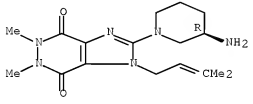
Absolute stereochemistry.



●2 HCl

RN 808736-78-9 HCAPLUS
CN 1H-Imidazo[4,5-d]pyridazine-4,7-dione, 2-[(3R)-3-amino-1-piperidinyl]-5,6-dihydro-5,6-dimethyl-1-(3-methyl-2-buten-1-yl)-, hydrochloride (1:2) (CA INDEX NAME)

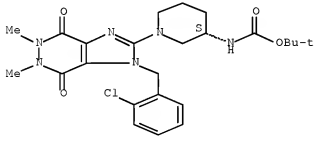
Absolute stereochemistry.



●2 HCl

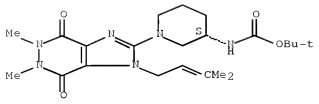
IT 808736-65-4P 808736-70-1P 808736-75-6P
808736-77-8P 808736-79-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 1H-imidazo[4,5-d]pyridazines as DPP-IV inhibitors for treatment of NIDDM)
RN 808736-65-4 HCAPLUS
CN Carbamic acid, [(3S)-1-[1-[(2-chlorophenyl)methyl]-4,5,6,7-tetrahydro-5,6-dimethyl-4,7-dioxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



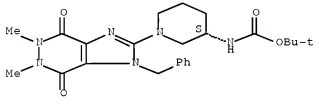
RN 808736-70-1 HCAPLUS
CN Carbamic acid, [(3S)-1-[4,5,6,7-tetrahydro-5,6-dimethyl-1-(3-methyl-2-butenyl)-4,7-dioxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



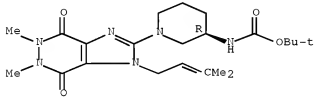
RN 808736-75-6 HCAPLUS
CN Carbamic acid, [(3S)-1-[4,5,6,7-tetrahydro-5,6-dimethyl-4,7-dioxo-1-(phenylmethyl)-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 808736-77-8 HCAPLUS
CN Carbamic acid, [(3R)-1-[4,5,6,7-tetrahydro-5,6-dimethyl-1-(3-methyl-2-butenyl)-4,7-dioxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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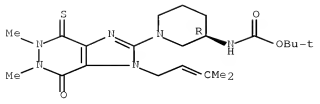
CN Carbamic acid, [(3R)-1-[4,5,6,7-tetrahydro-5,6-dimethyl-1-(3-methyl-2-butenyl)-7-oxo-4-thioxo-1H-imidazo[4,5-d]pyridazin-2-yl]-3-piperidinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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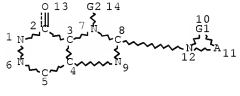

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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE
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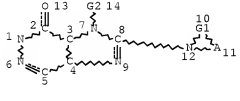

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VAR G2=AK/CY
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L11           2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 NOT L6
L12         246 SEA FILE=HCAPLUS ABB=ON  PLU=ON  YOSHIKAWA S/AU OR YOSHIKAWA S
                ?/AU OR YOSHIKAWA SEIJI/AU
L13          16 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("EMORI E"/AU OR "EMORI
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L14          48 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "MATSUURA F"/AU OR MATSUURA F
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L15        2821 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "CLARK RICHARD"/AU OR CLARK
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                L25 OR L26 OR L27 OR L28) NOT (L6 OR L11)


=> d ibib abs hitstr l29 1-35

L29  ANSWER 1 OF 35  HCAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:         2007:1387236  HCAPLUS  Full-text
DOCUMENT NUMBER:          148:528970
TITLE:                    Phase I Study of S-1 Combined with Irinotecan (CPT-11)
                          in Patients with Advanced Colorectal Cancer
AUTHOR(S):                Tsunoda, A.; Yasuda, N.; Nakao, K.; Narita, K.;
                          Yamazaki, K.; Watanabe, M.; Suzuki, N.; Kusano, M.
CORPORATE SOURCE:         Department of General and Gastroenterological Surgery,
                          Showa University School of Medicine, Tokyo, Japan
SOURCE:                   Oncology (2007), 72(1-2), 58-63
                          CODEN: ONCOBS; ISSN: 0030-2414
PUBLISHER:                S. Karger AG
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
```

AB Purpose: To determine the maximum tolerated dose, recommended dose and dose-limiting toxicities of irinotecan plus S-1 in advanced colorectal cancer. Patients and Methods: S-1 was administered orally at 80 mg/m2/day for 21 consecutive days followed by a 2-wk rest. CPT-11 was given i.v. on days 1 and 15 of each course, at an initial dose of 60 mg/m2/day, stepping up to 80, 100, 120 or 140 mg/m2/day. Courses were repeated every 5 wk, unless disease progression or severe toxicities were observed Results: A total of 20 patients were entered in this study. The maximum tolerated dose of CPT-11 was considered to be 100 mg/m2, because 2 of 3 patients developed dose-limiting toxicities, such as anorexia, fatigue and diarrhea. Therefore, the recommended dose of CPT-11 was set at 80 mg/m2. Tumor responses were seen in 8 of 14 patients with measurable lesions. Conclusion: A combination of S-1 with CPT-11 is safe and can be recommended for further phase II studies in patients with advanced colorectal cancer.

L29 ANSWER 2 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1114962 HCAPLUS Full-text
DOCUMENT NUMBER: 147:427349
TITLE: Preparation of triazolone derivatives as blood coagulation factor VIIa inhibitors
INVENTOR(S): Clark, Richard; Matsuura, Fumiyoshi; Kira, Kazunobu; Hirota, Shinsuke; Azuma, Hiroshi; Nagakura, Tadashi; Horizoe, Tatsuo; Tabata, Kimiyo; Kusano, Kazutomi; Omae, Takao; Inoue, Atsushi
PATENT ASSIGNEE(S): Eisai R & D Management Co., Ltd., Japan
SOURCE: PCT Int. Appl., 663pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007111212	A1	20071004	WO 2007-JP55813	20070322
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 20080015199	A1	20080117	US 2007-723893	20070322

PRIORITY APPLN. INFO.:		
JP 2006-83486	A	20060324
US 2006-786687P	P	20060329
JP 2006-162594	A	20060612
US 2006-804878P	P	20060615
JP 2006-218819	A	20060810
US 2006-838418P	P	20060818

OTHER SOURCE(S): MARPAT 147:427349
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds., i.e. 4-[[[(hetero)aryl](5-oxo-4,5-dihydro-1H-triazol-2-yl)methyl]amino]benzamidine derivs. [I; R1a, R1b, R1c, R1d = H, HO, C1-6 alkyl, halo; R2 = each (un)substituted C6-10 aryl, 5- to 10-membered heteroaryl, or 9- to 12-membered benzene-fused ring group; R3 = each (un)substituted 5- or 6-membered nonarom. heterocyclyl, C6-10 aryl, or 5- to 10-membered heteroaryl; Z1, Z2 = H], enantiomers thereof, salts thereof, and their hydrates are prepared These compds. show excellent inhibitory activity against blood coagulation factor VIIa and appropriate physicochem. stability and are useful as therapeutic agents and/or preventives for diseases caused by clot formation (thrombogenesis), in particular thrombosis, deep vain thrombosis, pulmonary thrombosis, cerebral infarction, myocardial infarction, acute coronary syndrome, vascular restenosis, disseminated intravascular coagulation, and malignant tumors. Thus, a solution of 90 mg [2-(8-Methoxy-4H-benzo[1,3]dioxin-6-yl)-2- [4-(5-methyl-[1,2,4]oxadiazol-3-yl)phenylimino]-1- methylsulfanylethylidene]carbamic acid Me ester in 1 mL DMF was treated with 32 mg 3-hydrazinothiophene-2-carboxylic acid Me ester and 0.030 mL Et3N, stirred at 85° for 20 h, concentrated, dissolved in 0.1 mL AcOH, 0.8 mL MeOH, and 0.8 mL THF, treated with 100 mg sodium cyanoborohydride, and stirred at room temperature for 18.5 h, followed by purification by HPLC to give a crude product. The crude product was stirred with 100 mg Fe powder in a 1:1:1 mixture of MeOH, H2O, and AcOH (3 mL), stirred at 65° for 16 h, followed by purification using reversed phase HPLC to give 3-(3-[(4-carbamimidoylphenylamino)(8-methoxy-4H-benzo[1,3]dioxin-6-yl)methyl]-5-oxo-4,5-dihydro-1H-[1,2,4]triazol-1-yl)thiophene-2-carboxylic acid Me ester acetate (II) which was separated by HPLC using a SUMICHIRAL OA-2500 column to give (R)- and (S)-II. II showed IC50 of 0.0012 μM against blood coagulation factor VIIa.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 3 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	2006:1286630 HCAPLUS Full-text
DOCUMENT NUMBER:	146:155856
TITLE:	7-But-2-ynyl-9-(6-methoxy-pyridin-3-yl)-6-piperazin-1-yl-7,9-dihydro-purin-8-one is a novel competitive and selective inhibitor of dipeptidyl peptidase IV with an antihyperglycemic activity
AUTHOR(S):	Yamazaki, Kazuto; Yasuda, Nobuyuki; Inoue, Takashi; Nagakura, Tadashi; Kira, Kazunobu; Shinoda, Masanobu; Saeki, Takao; Tanaka, Isao
CORPORATE SOURCE:	Tsukuba Research Laboratories, Eisai Co., Ltd., Ibaraki, Japan
SOURCE:	Journal of Pharmacology and Experimental Therapeutics (2006), 319(3), 1253-1257 CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER:	American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB 7-But-2-ynyl-9-(6-methoxy-pyridin-3-yl)-6-piperazin-1-yl-7,9-dihydro-purin- 8-one (ER-319711) is a novel dipeptidyl peptidase (DPP)-IV inhibitor discovered in our labs. In this study, we have characterized this DPP-IV inhibitor in vitro and in vivo as an antidiabetic agent. The trifluoroacetate salt form of

ER-319711, ER-319711-15, inhibited human DPP-IV with an IC50 value of 0.089 μM, whereas its IC50 values toward human DPP8 and DPP9 were >100 μM. Inhibition kinetic pattern anal. indicated that ER-319711-15 inhibited DPP-IV in a competitive manner. ER-319711-15 (1 mg/kg) reduced glucose excursion in an oral glucose tolerance test (OGTT) using Zucker fa/fa rats, with significant increases in plasma insulin and active glucagon-like peptide-1 levels. In an OGTT using mice fed a high-fat diet in which ER-319711-15 (0.1-10 mg/kg) was orally administered at 0 h, and glucose was loaded at 0 and 5 h, this compound improved glucose tolerance dose dependently at both 0- and 5-h glucose loading. Next, we compared efficacy of ER-319711-15, E3024, a competitive DPP-IV inhibitor having an imidazopyridazinone structure, or vildagliptin, a slow-binding and long-acting DPP-IV inhibitor, at the same dose, 10 mg/kg, in the same procedures. At the first glucose challenge, all compds. lowered area under the curve (AUC) values of delta blood glucose between 0 and 2 h significantly to the same degree. At the second glucose load, the AUC values between 5 and 7 h were significantly decreased by ER-319711-15 and vildagliptin, but not by E3024. Therefore, ER-319711 might be a potent, competitive, and selective DPP-IV inhibitor with an antihyperglycemic activity.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 4 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:366878 HCAPLUS Full-text

DOCUMENT NUMBER: 144:412379

TITLE: Preparation of 2-(4-carbamimidoylphenylamino)-2-phenylacetic acid hydrazide derivatives as preventives or therapeutic agents for diseases caused by thrombus formation

INVENTOR(S): Clark, Richard; Hirota, Shinsuke; Azuma, Hiroshi; Kira, Kazunobu; Watanabe, Nobuhisa; Nagakura, Tadashi; Horizoe, Tatsuo

PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan

SOURCE: PCT Int. Appl., 281 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

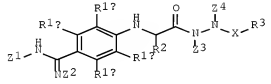
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006041119	A1	20060420	WO 2005-JP18853	20051013
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
EP 1810965	A1	20070725	EP 2005-793650	20051013
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL,			

BA, HR, MK, YU

US 20080132507 A1 20080605 US 2007-665385 20070413
PRIORITY APPLN. INFO.: JP 2004-298379 A 20041013
WO 2005-JP18853 W 20051013

OTHER SOURCE(S): MARPAT 144:412379

GI



I

AB Compds. represented by the general formula (I) or salts thereof, or hydrates of both [R1a, R1b, R1c, R1d = H, halo, C1-6 alkyl; R2 = (un)substituted Ph; R3 = H, C1-6, each (un)substituted C3-8 cycloalkyl, 5- or 6-membered nonarom. heterocyclyl, C6-10 aryl, 5- or 6-membered heteroaryl, C6-10 arylmethyl, C6-10 arylamino, 5- to 10-membered heteroarylmethyl, or 5- to 10-membered heteroarylamino; Z1, Z2, Z3 = H, C1-6 alkyl; X = a single bond, S(O)2, CO, C(S)] are prepared These compds. are safe and have moderate physicochem. stability and useful as preventive or therapeutic agents for diseases caused by thrombus formation including thrombosis, deep venous thrombosis, pulmonary embolism, cerebral infarction, myocardial infarction, vascular restenosis, disseminated intravascular coagulation, and malignant tumor. Thus, a mixture of 3-chloroisonicotinic acid 5.2, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimi de hydrochloride 6.1, 1-hydroxybenzotriazole monohydrate 4.9, and 0.6 mL DMF was stirred at 0° for 1 h, treated with 15 mg 4-[[[[N'-[3-ethoxy-4-(2-methoxyethoxy)phenyl]hydrazino]carbonyl]methyl]ami no]benzamidine dihydrochloride, and stirred at room temperature overnight to give 28% 4-[[2-[N'-[(3-Chloropyridin-4-yl)carbonyl]hydrazino]-1-[3-ethoxy- 4-(2-methoxyethoxy)phenyl]-2-oxoethyl]amino]benzamidine trifluoroacetate (II). II in vitro showed IC50 of 0.049 mM against blood coagulation factor VIIa.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 5 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:561821 HCAPLUS Full-text
DOCUMENT NUMBER: 143:52541
TITLE: Therapeutic potential of DPP-IV inhibitor for the treatment of type 2 diabetes
AUTHOR(S): Yasuda, Nobuyuki; Yamazaki, Kazuto; Inoue, Takashi; Nagakura, Tadashi
CORPORATE SOURCE: Tsukuba Res. Lab., Eisai Co., Ltd., Tsukuba, 300-2635, Japan
SOURCE: Nippon Yakurigaku Zasshi (2005), 125(6), 379-384
CODEN: NYKZAU; ISSN: 0015-5691
PUBLISHER: Nippon Yakuri Gakkai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review on development and pharmacol. and clin. effects of antidiabetic dipeptidyl peptidase-IV (DPP-IV) inhibitors which enhance glucagon-like peptide-1 (GLP-1) action, discussing the structure, secretion, and metabolism of GLP-1, pharmacol. actions of GLP-1, inactivation of GLP-1 by DPP-IV,

involvement of DPP-IV in diabetes mellitus, and effects and adverse effect of DPP-IV inhibitors for treatment of type 2 diabetes mellitus.

L29 ANSWER 6 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:658129 HCAPLUS Full-text
TITLE: Novel piperazine-substituted, heterocyclic compounds as selective, competitive DPP-IV inhibitors
AUTHOR(S): Clark, Richard S. J.; Matsuura, Fumiyoshi; Kira, Kazunobu; Yoshikawa, Seiji; Ikuta, Hironori; Yasuda, Nobuyuki; Nagakura, Tadashi; Yamazaki, Kazuto; Takenaka, Osamu
CORPORATE SOURCE: Frontier Research Laboratory, Eisai Co.Ltd, Tsukuba, 300-2635, Japan
SOURCE: Abstracts of Papers, 228th ACS National Meeting, Philadelphia, PA, United States, August 22-26, 2004 (2004), MEDI-265. American Chemical Society: Washington, D. C.
CODEN: 69FTZ8
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB GLP-1 is an incretin released from L cells in the gut in response to the oral ingestion of nutrients. It has multiple actions contributing to normalization of elevated blood glucose levels, but is rapidly processed by dipeptidyl peptidase IV (DPP-IV), leading to an extremely short active half-life. Inhibition of DPP-IV is therefore expected to be beneficial in the treatment of diabetes. A compound identified from HTS of an inhouse library was developed into several series of potent and selective DPP-IV competitive inhibitors, leading to the identification of several promising candidates for clin. introduction. This poster will describe the SARs for these compds., and also outline their biol. properties.

L29 ANSWER 7 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:658126 HCAPLUS Full-text
TITLE: Development of a novel inhibitor of DPP-IV using a byproduct as the lead compound
AUTHOR(S): Kira, Kazunobu; Clark, Richard S. J.; Ikuta, Hironori; Yoshikawa, Seiji; Yasuda, Nobuyuki; Yamazaki, Kazuto; Nagakura, Tadashi; Takenaka, Osamu; Uehara, Taisuke
CORPORATE SOURCE: Frontier Research Laboratory, Eisai Co.Ltd, Tsukuba, 300-2635, Japan
SOURCE: Abstracts of Papers, 228th ACS National Meeting, Philadelphia, PA, United States, August 22-26, 2004 (2004), MEDI-262. American Chemical Society: Washington, D. C.
CODEN: 69FTZ8
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB GLP-1 is an incretin released from L cells in the gut in response to the oral ingestion of nutrients. It has multiple actions contributing to normalization of elevated blood glucose levels, but is rapidly processed by dipeptidyl peptidase IV (DPP-IV), leading to an extremely short active half-life. Inhibition of DPP-IV is therefore expected to be beneficial in the treatment of diabetes. As part of an effort to develop novel inhibitors of DPP-IV, a systematic study using a byproduct (produced during the large scale synthesis of ER-260891) as a lead compound has been performed and resulted in some

promising compds. It should be noted that a byproduct (only 0.34 % yield) changed into a powerful lead compound

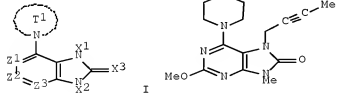
L29 ANSWER 8 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:608730 HCAPLUS Full-text
DOCUMENT NUMBER: 141:236194
TITLE: Metformin causes reduction of food intake and body weight gain and improvement of glucose intolerance in combination with dipeptidyl peptidase IV inhibitor in Zucker fa/fa rats
AUTHOR(S): Yasuda, Nobuyuki; Inoue, Takashi; Nagakura, Tadashi; Yamazaki, Kazuto; Kira, Kazunobu; Saeki, Takao; Tanaka, Isao
CORPORATE SOURCE: Tsukuba Research Laboratories, Eisai Co., Ltd., Tsukuba, Japan
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2004), 310(2), 614-619
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An incretin hormone, glucagon-like peptide-1 (GLP-1), has been shown to lower plasma glucose via glucose-dependent insulin secretion and to reduce appetite. The authors previously found that the biguanide metformin, an antidiabetic agent, causes a significant increase of plasma active GLP-1 level in the presence of dipeptidyl peptidase IV (DPPIV) inhibitor in normal rats. This finding suggested that the combination treatment might produce a greater antidiabetic and anorectic effect, based on enhanced GLP-1 action. In this study, the authors assessed the effects of subchronic treatment with metformin and a DPPIV inhibitor, valine-pyrrolidide (val-pyr), on glycemic control, food intake, and weight gain using Zucker fa/fa rats, a model of obesity and impaired glucose tolerance. The combination treatment caused a significant increase of GLP-1 level in Zucker fa/fa rats. In a subchronic study, val-pyr, metformin, or both compds. were administered orally b.i.d. for 14 days. The combination treatment significantly decreased food intake and body weight gain, although neither metformin nor val-pyr treatment alone had any effect. In an oral glucose tolerance test on day 1, the coadministration caused a greater improvement of glucose tolerance and a prominent increase of plasma active GLP-1 without marked insulin secretion. The 14-day combination treatment produced a potent reduction of fasting blood glucose and plasma insulin levels. These results demonstrate that the combination therapy of metformin with DPPIV inhibitor leads to reduced food intake and body weight gain, most likely through the significant increase of plasma GLP-1 level. The combination therapy seems to be a good candidate for treatment of type 2 diabetes with obesity.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 9 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:493703 HCAPLUS Full-text
DOCUMENT NUMBER: 141:54356
TITLE: Preparation of 1,3-dihydroimidazole fused-ring compounds as dipeptidylpeptidase IV (DPP-IV) inhibitors
INVENTOR(S): Kira, Kazunobu; Clark, Richard; Yoshikawa, Seiji; Uehara, Taisuke

PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: PCT Int. Appl., 143 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004050656	A1	20040617	WO 2003-JP15402	20031202
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2507763	A1	20040617	CA 2003-2507763	20031202
AU 2003302657	A2	20040623	AU 2003-302657	20031202
AU 2003302657	A1	20040623		
EP 1568699	A1	20050831	EP 2003-812368	20031202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003016991	A	20051025	BR 2003-16991	20031202
CN 1745080	A	20060308	CN 2003-80109519	20031202
NZ 540495	A	20070928	NZ 2003-540495	20031202
MX 2005PA05983	A	20050818	MX 2005-PA5983	20050603
ZA 2005004973	A	20060426	ZA 2005-4973	20050620
NO 2005003246	A	20050830	NO 2005-3246	20050701
IN 2005CN01470	A	20070622	IN 2005-CN1470	20050701
US 20060111362	A1	20060525	US 2005-537227	20051227
PRIORITY APPLN. INFO.:			JP 2002-352186 A	20021204
			WO 2003-JP15402 W	20031202

OTHER SOURCE(S): MARPAT 141:54356
GI



I II

AB Title compds. I [wherein T1 = (un)substituted 1-2 nitrogen containing cyclic ring; X1 = (un)substituted alkyl, alkenyl, (hetero)allyl, etc.; X3 = O, S, (un)substituted amino; Z1 = N or CR3; Z2, Z3 = independently N, CR1, CO, NR2; R1-R3, X2 = H, (un)substituted heterocyclic ring or (un)substituted alkylene; and their salts or hydrates thereof] were prepared as dipeptidylpeptidase IV

(DPP-IV) inhibitors. For example, II•CF3CO2H was prepared in 6-steps synthesis starting from 3,7-dihydro-3-methyl-1H- purine-2,6-dione. I showed DPP-IV inhibition with the IC50 value of 0.0029-89.5 μM. Thus, I and their pharmaceutical compns. are useful as DPP-IV inhibitors for the treatment of diabetes mellitus, obesity, hyperlipemia, and etc. (no data).

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 10 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:243596 HCAPLUS Full-text

DOCUMENT NUMBER: 140:368426

TITLE: The combination of metformin and a dipeptidyl peptidase IV inhibitor prevents 5-fluorouracil-induced reduction of small intestine weight

AUTHOR(S): Yamazaki, Kazuto; Yasuda, Nobuyuki; Inoue, Takashi; Nagakura, Tadashi; Kira, Kazunobu; Saeki, Takao; Tanaka, Isao

CORPORATE SOURCE: Tsukuba Research Laboratories, Eisai Co., Ltd., 5-1-3, Tokodai, Ibaraki, Tsukuba, 300-2635, Japan

SOURCE: European Journal of Pharmacology (2004), 488(1-3), 213-218
CODEN: EJPHAZ; ISSN: 0014-2999

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Glucagon-like peptide 2 (GLP-2), which has intestinotrophic effects, is secreted from L-cells in the intestine in response to nutrient ingestion and is degraded by dipeptidyl peptidase IV (DPPIV). In this report, we show that biguanides promote GLP-2 release. Plasma GLP-2 levels were significantly increased by 1.4- to 1.6-fold in fasted F344 rats 1 h after oral meformin (300 mg/kg), phenformin (30 and 100 mg/kg) and buformin (100 mg/kg) treatment. In addition, metformin administration (300 mg/kg, p.o.) significantly elevated plasma GLP-2 in fasted CD-1 mice by about 2.0-fold 1 and 3 h after the treatment. Metformin and/or valine-pyrrolidide, a DPPIV inhibitor, was orally given (300 and 30 mg/kg, resp., p.o., b.i.d., 3 days) to BALB/c mice treated with 5-fluorouracil (5-FU; 60 mg/kg, s.i.d.), which induces gastrointestinal damage leading to a reduction of small intestine wet weight Metformin and valine-pyrrolidide co-administration prevented the 5-FU-induced reduction of wet weight of the small intestine, whereas metformin or valine-pyrrolidide alone had no effect. These results suggest that GLP-2 is co-secreted with GLP-1 flollowing biguanide stimulation, and that the combination of metformin with a DPPIV inhibitor might a useful oral treatment for gastrointestinal damage, based on GLP-2 actions.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 11 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:226443 HCAPLUS Full-text

TITLE: Discovery and optimization of potent orally active small molecular thrombin receptor(PAR-1) antagonists

AUTHOR(S): Kawahara, Tetsuya; Suzuki, Shuichi; Matsuura, Fumiyoshi; Clark, Richard S. J.; Kogushi, Motoji; Kobayashi, Hiroko; Hishinuma, Ieharu; Sato, Nobuaki; Terauchi, Taro; Kajiwara, Akiharu; Matsuoka, Toshiyuki

CORPORATE SOURCE: Frontier Research Laboratories, Eisai Co., Ltd., Tsukuba, 300-2635, Japan

SOURCE: Abstracts of Papers, 227th ACS National Meeting, Anaheim, CA, United States, March 28-April 1, 2004

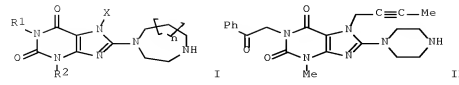
(2004), MEDI-085. American Chemical Society: Washington, D. C.
CODEN: 69FGKM
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English

AB Thrombin, a trypsin-like serine protease, is centrally involved in hemostasis, and also promotes diverse cellular responses such as platelet aggregation, lymphocyte mitosis, monocyte chemotaxis, and vascular smooth muscle proliferation. These actions are mediated by proteolytically- activated thrombin receptors (protease-activated receptors: PARs). A non-peptide small mol. PAR-1 antagonist (ER-97719-15) was obtained from high throughput screening using a receptor binding assay system. Through optimization of ER-97719-15, we found three types of compound with moderate PAR-1 antagonistic activity. In particular the indolin derivative ER-121958-06 inhibited human PRP aggregation by thrombin at 21nM. ER-121958-06(10 mg/kg p.o.) inhibited ex vivo aggregation induced by thrombin in the guinea pig. Furthermore ER-129614-06 (100 mg/kg, p.o.) prolonged the time to occlusion in the irradiated artery by 1.9 fold compared to control. In this PIT (photochem.-induced thrombosis) model, ER129614-06 selectively inhibited thrombin-induced PRP aggregation ex vivo. The SAR and biol. evaluation of this series of compds. are described.

L29 ANSWER 12 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:675555 HCAPLUS Full-text
DOCUMENT NUMBER: 139:197299
TITLE: Preparation of xanthine derivatives as DPP-IV inhibitors
INVENTOR(S): Yoshikawa, Seiji; Emori, Eita; Matsuura, Fumiyoshi; Clark, Richard; Ikuta, Hironori; Yasuda, Nobuyuki; Nagakura, Tadashi; Yamataki, Kazuto; Aoki, Mika
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 217 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1338595	A2	20030827	EP 2003-290431	20030224
EP 1338595	A3	20031008		
EP 1338595	B1	20060503		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2004043429	A	20040212	JP 2003-44771	20030221
US 20040082570	A1	20040429	US 2003-374918	20030224
US 7074798	B2	20060711		
PRIORITY APPLN. INFO.:			JP 2002-47761 A	20020225
			JP 2002-149557 A	20020523
OTHER SOURCE(S):	MARPAT 139:197299			

GI



I II

AB Novel xanthine derivs. of formula I [R1, R2 = H, alkyl, alkoxy, hydroxyalkyl, cycloalkyl, aryl, etc.; X = alkynyl, (substituted) Ph; n = 0, 1] are prepared which exhibit an excellent dipeptidyl peptidase IV (DPPIV) inhibition effect. Thus, II was prepared, and inhibited DPPIV with IC50 of 0.654 nM, and improved glucose tolerance in mice by 49.4%.

L29 ANSWER 13 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:154391 HCAPLUS Full-text
DOCUMENT NUMBER: 138:187634
TITLE: Preparation of 2-benzyltetrahydrofuran-2-carboxylic acid derivatives as PPAR agonists for treatment of hyperglycemia, hyperlipemia, and inflammatory diseases
INVENTOR(S): Clark, Richard; Matsuura, Fumiyoshi; Emori, Eita; Shinoda, Masanobu; Kasai, Shunji; Yoshitomi, Hideki; Yamazaki, Kazuto; Inoue, Takashi; Miyashita, Sadakazu; Hihara, Taro
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: PCT Int. Appl., 220 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003016265	A1	20030227	WO 2002-JP8325	20020816
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002325535	A1	20030303	AU 2002-325535	20020816
EP 1452521	A1	20040901	EP 2002-758850	20020816
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 20050014833	A1	20050120	US 2004-486396	20040211
US 7371777	B2	20080513		
PRIORITY APPLN. INFO.:			JP 2001-247540	A 20010817
			WO 2002-JP8325	W 20020816

OTHER SOURCE(S): MARPAT 138:187634
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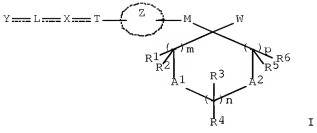
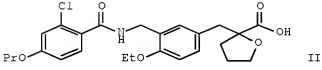


I



II

AB The title compds. I [wherein m, n, and p = independently 0-4; R1-R6 = independently H, OH, CN, halo, NR7R8, (un)substituted alkyl(thio), alkoxy, HO-alkyl(thio), HO-alkoxy, aminoalkyl(thio), halo-alkyl(thio), halo-alkoxy, alkoxyalkyl(thio), alkoxyalkoxy, cycloalkyl(oxy), cycloalkylalkyloxy, cycloalkylthio, alkenyl(oxy), alkenylthio, alkynyl(oxy), alkynylthio, aryl(oxy), arylthio, alkylaryl(oxy), alkylarylthio, aralkyl(oxy), or aralkylthio; R7 and R8 = independently H, CN, CHO, (un)substituted (amino)alkyl, HO-alkyl, halo-alkyl, alkoxyalkyl, cycloalkyl, alkenyl, alkynyl, (alkyl)aryl, aralkyl, acyl, or alkoxy-CO; A1 and A2 = independently a single bond, O, S, SO, SO2, (un)substituted amino, or alkenylenyl; L, M, and T = independently a single bond, (un)substituted alkylenyl, alkenylenyl, or alkynylenyl; W = CO2H; X = a single bond, O, OSO2, SO3, (un)substituted amino(thio)carboxy, (thio)carbamato, (thio)carbamoyloxy, (oxy)amino(thio)carbonyl, (amino)(thio)carbamoyl, aminosulfonyl, or sulfonamido; Y = (un)substituted Ar(Ar); Ar = aromatic ring; ring Z = (un)substituted Ar] and salts, esters, and hydrates thereof are prepared as PPAR (peroxisome proliferator-activated receptor) agonists for the treatment of hyperglycemia, hyperlipemia, and inflammatory diseases. For example, the acid II was prepared in a multi-step synthesis starting from 2-chloro-4-propoxybenzoic acid and the corresponding amine (prepn given) in DMF in the presence of Et3N and di-Et cyanophosphonate. II showed EC50 of 0.013, 0.038, and 0.005 μM against PPAR α, PPAR β, and PPAR γ, resp.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 14 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:57732 HCAPLUS Full-text

DOCUMENT NUMBER: 139:30524

TITLE: Squalene synthase inhibitors suppress triglyceride biosynthesis through the farnesol pathway in rat hepatocytes

AUTHOR(S): Hiyoshi, Hironobu; Yanagimachi, Mamoru; Ito, Masashi; Yasuda, Nobuyuki; Okada, Toshimi; Ikuta, Hironori; Shinmyo, Daisuke; Tanaka, Keigo; Kurusu, Nobuyuki; Yoshida, Ichiro; Abe, Shinya; Saeki, Takao; Tanaka, Hiroshi

CORPORATE SOURCE: Tsukuba Research Laboratories, Eisai Co. Ltd.,

Ibaraki, Japan
SOURCE: Journal of Lipid Research (2003), 44(1), 128-135
CODEN: JLPRAW; ISSN: 0022-2275
PUBLISHER: Lipid Research, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We recently demonstrated that squalene synthase (SQS) inhibitors reduce plasma triglyceride through an LDL receptor-independent mechanism in Watanabe heritable hyperlipidemic rabbits. The present study deals with the mechanism of the inhibition of triglyceride biosynthesis by the SQS inhibitors ER-27856 and RPR-107393 in rat primary cultured hepatocytes. Atorvastatin, an HMG-CoA reductase inhibitor, had no effect on triglyceride biosynthesis, but reversed the inhibitory effect of the SQS inhibitors. A squalene epoxidase inhibitor, NB-598, affected neither triglyceride biosynthesis nor its inhibition by ER-27856 and RPR-107393. The reduction of triglyceride biosynthesis by ER-27856 and RPR-107393 was potentiated by mevalonolactone supplementation. Treatment of hepatocytes with farnesol and its derivs. reduced triglyceride biosynthesis. In addition, we found that ER-27856 and RPR-107393 significantly reduced the incorporation of [1-14C]acetic acid into oleic acid, but not the incorporation of [1-14C]oleic acid into triglyceride. Though ER-27856 and RPR-107393 increased mitochondrial fatty acid β-oxidation, the inhibition of β-oxidation by RS-etomoxir had little effect on their inhibition of triglyceride biosynthesis. These results suggest that SQS inhibitors reduce triglyceride biosynthesis by suppressing fatty acid biosynthesis via an increase in intracellular farnesol and its derivs.
REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 15 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:26816 HCAPLUS Full-text
DOCUMENT NUMBER: 139:46829
TITLE: Enteroinsular axis of db/db mice and efficacy of dipeptidyl peptidase IV inhibition
AUTHOR(S): Nagakura, Tadashi; Yasuda, Nobuyuki; Yamazaki, Kazuto; Ikuta, Hironori; Tanaka, Isao
CORPORATE SOURCE: Tsukuba Research Laboratories, Eisai Co. Ltd, Ibaraki, 300-2635, Japan
SOURCE: Metabolism, Clinical and Experimental (2003), 52(1), 81-86
CODEN: METAAJ; ISSN: 0026-0495
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In type 2 diabetic patients, the administration of glucagon-like peptide-1 (GLP-1), known as an incretin, exerts antidiabetic effects. However, GLP-1 is rapidly degraded by dipeptidyl peptidase IV (DPPIV) after its release. DPPIV inhibition is thought to be a rational strategy to treat type 2 diabetes. In this study, using C57BLKS/J-db/db (db/db) mice as a model of type 2 diabetes, we examined the effect of acute DPPIV inhibition on glucose tolerance at the early and later stages of diabetes, determining plasma active GLP-1 and insulin levels. In addition, we investigated changes of plasma DPPIV activity. Compared with normal C57BL6/J (B6) and db/+ mice, significantly increased plasma DPPIV activities were observed in db/db mice. Expression of the proglucagon gene encoding GLP-1 was significantly upregulated in the colon of db/db mice. The administration of valine-pyrrolidide, a DPPIV inhibitor, resulted in potentiated insulin secretion mediated by increased endogenous GLP-1 action, leading to improved glucose tolerance in db/db mice at 6 wk of age. However, although acute DPPIV inhibition with valine-pyrrolidide

resulted in higher plasma active GLP-1 and insulin levels in db/db mice at 23 wk of age, it did not improve glucose tolerance. The function of the enteroinsular axis is preserved in both stage of diabetes and the DPPIV inhibitor potentiated it, but the progression of insulin resistance appeared to block the improvement of glucose tolerance through DPPIV inhibition. Our results suggest that DPPIV inhibition is a suitable approach for treatment of impaired glucose tolerance (IGT), and type 2 diabetes in the early stage.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 16 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:8039 HCAPLUS Full-text
DOCUMENT NUMBER: 138:332031
TITLE: Functional characterization of the adenosine receptor contributing to glycogenolysis and gluconeogenesis in rat hepatocytes
AUTHOR(S): Yasuda, Nobuyuki; Inoue, Takashi; Horizoe, Tatsuo; Nagata, Kaya; Minami, Hiroe; Kawata, Tsutomu; Hoshino, Yorihisa; Harada, Hitoshi; Yoshikawa, Seiji; Asano, Osamu; Nagaoka, Junsaku; Murakami, Manabu; Abe, Shinya; Kobayashi, Seiichi; Tanaka, Isao
CORPORATE SOURCE: Tsukuba Research Laboratories, Eisai Co. Ltd., 5-1-3 Tokodai, Tsukuba, Ibaraki, 300-2635, Japan
SOURCE: European Journal of Pharmacology (2003), 459(2-3), 159-166
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The adenosine receptor subtype mediating glucose production by glycogenolysis and gluconeogenesis was studied in primary cultured rat hepatocytes. Adenosine and adenosine agonists caused cAMP accumulation in rat hepatocytes. The order of potency was 5'-N-ethylcarboxamidoadenosine (NECA)>R(-)-N6-(2-phenylisopropyl)adenosine (RPIA)>adenosine>2-[p-(carboxyethyl)phenylethylamino]-5'-N-ethylcarboxamidoadenosine (CGS21680). Furthermore, adenosine agonists stimulated glycogenolysis and gluconeogenesis. The order of potency was NECA>RPIA>CGS21680. The rank order of potency is typical for adenosine A2B receptors. Glycogenolysis stimulated by NECA was fully inhibited by nonselective adenosine antagonists, 9-chloro-2-(2-furanyl)[1,2,4]triazolo[1,5-c]quinazolin-5- amine (CGS15943). However, the adenosine A2A receptor-selective antagonist, 8-(3-chlorostyryl)caffeine (CSC), and the adenosine A1 receptor-selective antagonist, (+)-(R)-[(E)-3-(2-phenylpyrazolo[1,5- alpha]pyridin-3-yl)acryloyl]-2-piperidine ethanol (FK453), had a low inhibitory potency. A strong correlation was found between the inhibitory effect of adenosine antagonists on NECA-induced glucose production and that on intracellular cAMP generation in rat hepatocytes. The authors' results suggest that adenosine stimulates cAMP formation and regulates glycogenolysis and gluconeogenesis, most likely through the adenosine A2B receptor subtype in rat hepatocytes.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 17 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:964312 HCAPLUS Full-text
DOCUMENT NUMBER: 138:39105
TITLE: Preparation of phenylpropionic acid and indolylpropionic acid derivatives and salt thereof as dual or triple agonists of peroxisome

proliferator-activated receptors (PPAR)

INVENTOR(S): Matsuura, Fumiyoshi; Emori, Eita; Shinoda, Masanobu; Clark, Richard; Kasai, Shunji; Yoshitomi, Hideki; Yamazaki, Kazuto; Inoue, Takashi; Miyashita, Sadakazu; Hihara, Taro; Harada, Hitoshi; Ohashi, Kaya

PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan

SOURCE: PCT Int. Appl., 404 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002100812	A1	20021219	WO 2002-JP3866	20020418
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2442319	A1	20021219	CA 2002-2442319	20020418
AU 2002251481	A1	20021223	AU 2002-251481	20020418
AU 2002251481	B2	20070809		
EP 1380562	A1	20040114	EP 2002-720489	20020418
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
HU 2003003810	A2	20040301	HU 2003-3810	20020418
CN 1503774	A	20040609	CN 2002-808498	20020418
BR 2002009027	A	20050524	BR 2002-9027	20020418
NZ 539708	A	20050930	NZ 2002-539708	20020418
NZ 528655	A	20051223	NZ 2002-528655	20020418
RU 2316537	C2	20080210	RU 2003-133744	20020418
ZA 2003006895	A	20051003	ZA 2003-6895	20030903
IN 2003MN00841	A	20050429	IN 2003-MN841	20030908
NO 2003004669	A	20031217	NO 2003-4669	20031017
MX 2003PA09565	A	20040212	MX 2003-PA9565	20031017
US 20040102634	A1	20040527	US 2003-472543	20031022
ZA 2005007922	A	20060726	ZA 2005-7922	20050930

PRIORITY APPLN. INFO.:	JP 2001-123346	A	20010420
	JP 2002-36274	A	20020214
	WO 2002-JP3866	W	20020418

OTHER SOURCE(S): MARPAT 138:39105

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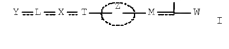

I

AB Carboxylic acid derivs. represented by general formula (I), salts or esters thereof, or hydrates thereof [wherein R1 = H, HO, halo, CO2H, each (un)substituted C1-6 alkyl, C1-6 alkoxy, C1-6 alkylthio, C1-6 hydroxyalkyl, C1-6 hydroxyalkoxy, C1-6 hydroxyalkylthio, C1-6 aminoalkyl, C1-6 aminoalkoxy, C1-6 aminoalkylthio, C1-6 haloalkyl, C1-6 haloalkoxy, C1-6 haloalkylthio, C2-12 alkoxyalkyl, C2-12 alkoxyalkoxy, C2-12 alkoxyalkylthio, C3-7 cycloalkyl, C3-7 cycloalkoxy, etc.; L, M = a single bond, each (un)substituted C1-6 alkylene, C2-6 alkenylene, or C2-6 alkynylene; T = a single bond, each (un)substituted C1-3 alkylene, C2-3 alkenylene, or C2-3 alkynylene; W = CO2H; a solid line accompanied by a dotted line represents a single or double bond; X = a single bond, O, N-(un)substituted NHCQlO, OCQlNH, CQlNHO, ONHCQ1, Q2SO2, SO2Q2, etc., wherein [Q1 = O, S; Q2 = O, (un)substituted NH]; Y = 5 to 14-membered aromatic group or C3-7 alicyclic hydrocarbon group optionally having ≥1 heteroatoms and ≥1 substituents; the ring Z = 5 to 14-membered aromatic group optionally having 1-4 substituents and ≥1 heteroatoms wherein a part of the ring is optionally saturated] are prepared These compds. are dual agonists of PPAR α and γ and triple agonists of PPAR α, β(δ), and γ and are useful as ameliorants (improvers) of insulin resistance, hypolipidemics, anti-osteoporosis agents, antiinflammatory agents, immunomodulators, and anticancer agents, and preventives and/or remedies for diabetes, diabetes complications, fragile X syndrome, hyperlipidemia, obesity, and digestive tract (gastrointestinal) diseases. The gastrointestinal diseases include (1) gastrointestinal inflammations such as ulcerative colitis, Crohn's disease, pancreatitis, and gastritis, (2) gastrointestinal proliferative diseases such as gastrointestinal benign tumors, gastrointestinal polyp, familial polyposis syndrome, colon cancer, rectal cancer, and stomach cancer, (3) gastrointestinal ulcers. They are also preventives and/remedies for (1) angina pectoris or myocardial infarction or its after effect of disease (sequelae), (2) senile dementia, and (3) cerebral vascular dementia based on improving energy metabs. Thus, 2,4-dichloroiodobenzene was coupled with Et 2-isopropoxy-3-[3-(2- propynyloxy)phenyl]propanoate in the presence of (Ph3P)4Pd, CuI, and Et3N in DMF at room temperature for 2 days followed by hydrolysis with a mixture of 5 N aqueous NaOH and MeOH and acidification with 1 N aqueous HCl, 2-isopropoxy-3-[3-[3- (2,4-dichlorophenyl)-2-propynyl]oxyphenyl]propanoic acid (II). II showed EC50 of 0.008, 1.249, and 0.008 nM for increasing the transcription of human PPAR α, β, and γ, resp., in yeast transfected with GAL4-PPAR LBD chimera expression vector.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 18 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:946252 HCAPLUS Full-text

DOCUMENT NUMBER: 138:39276

TITLE: Preparation of heterocyclecarboxylic acid, benzoic acid, and phenylalkanoic acid derivatives as agonists of peroxisome proliferator-activated receptors (PPAR)

INVENTOR(S): Matsuura, Fumiyoshi; Emori, Eita; Shinoda, Masanobu; Clark, Richard; Kasai, Shunji; Yoshitomi, Hideki; Yamazaki, Kazuto; Inoue, Takashi; Miyashita, Sadakazu; Hihara, Taro

PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan

SOURCE: PCT Int. Appl., 293 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002098840	A1	20021212	WO 2002-JP5511	20020604
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002306235	A1	20021216	AU 2002-306235	20020604
EP 1394147	A1	20040303	EP 2002-733294	20020604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 20040214888	A1	20041028	US 2003-479427	20031203
PRIORITY APPLN. INFO.:			JP 2001-168356 A	20010604
			WO 2002-JP5511 W	20020604
OTHER SOURCE(S):	MARPAT 138:39276			

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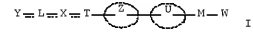

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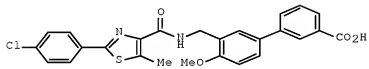

II

AB Novel carboxylic acid derivs. represented by the following general formula (I) [wherein L, M = a single bond, each (un)substituted C1-6 alkylene, C2-6 alkenylene, or C2-6 alkynylene; T = a single bond, each (un)substituted C1-3 alkylene, C2-3 alkenylene, or C2-3 alkynylene; W = CO2H; each solid line accompanied by a dotted line represents a single or double bond; X = a single bond, O, each N-(un)substituted NHCO-O, NHC(S)-O, O-CONH, O-C(S)NH, CONHO, C(S)NHO, ONHCO, ONHC(S), NHCO, NHC(S), CONH, C(S)NH, NHCONH, NHC(S)NH, NHSO2, or SO2NH, OSO2, SO2O, etc.; Y = 5 to 14-membered aromatic group or C3-7 alicyclic hydrocarbon group each optionally having ≥1 substituents or ≥1 heteroatoms; the ring Z or U = 5 to 14-membered aromatic group optionally having 1-4 substituents or ≥1 heteroatoms wherein a part of the ring is optionally saturated], salts or esters thereof, or hydrates thereof are prepared These compds. are dual agonists of PPAR α and γ or triple agonists of PPAR α, β(δ), and γ and useful as insulin resistance ameliorants, preventives and/or remedies for diabetes, fragile X syndrome, diabetes complications, hyperlipidemia, obesity, digestive tract diseases, and cancer. The digestive tract (gastrointestinal) diseases include (1) gastrointestinal inflammations such as ulcerative colitis, Crohn's disease, pancreatitis, and gastritis, (2) gastrointestinal proliferative diseases such as gastrointestinal benign tumor, polyp, hereditary polyposis, colon cancer, rectal cancer, and stomach cancer, and (3) gastrointestinal ulcer. They are also preventives and/or remedies for angina pectoris and myocardial infarction and sequelae thereof, senile

dementia, and cerebral vascular dementia based on the improvement effects on energy metabolism These compds. are also useful as hypolipidemics, anti-osteoporosis agents, antiinflammatory agents, and immunomodulators. For example, 3-[4-methoxy-3-[[[[4-methyl-2- (4-chlorophenyl)-1,3-thiazol-5-yl]carbonyl]amino]methyl]phenyl]benzoic acid (II) showed EC50 of <0.0001, 0.176, and 0.711 for the transcription activity of human PPAR in host CV-1 cells transfected with GAL4-PPAR LBD chimera expression vector.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 19 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:886010 HCAPLUS Full-text
DOCUMENT NUMBER: 137:370094
TITLE: Preparation of N-carbamoylazoles as dipeptidyl peptidase IV inhibitors.
INVENTOR(S): Yasuda, Nobuyuki; Nagakura, Tadashi; Yamazaki, Kazuto; Yoshikawa, Seiji; Okada, Toshimi; Ikuta, Hironori; Koyanagi, Mika
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 44 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1258480	A1	20021120	EP 2002-10252	20020517
EP 1258480	B1	20041110		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003034639	A	20030207	JP 2002-135555	20020510
US 20030060494	A1	20030327	US 2002-147105	20020515
ES 2231609	T3	20050516	ES 2002-10252	20020517
US 20040186153	A1	20040923	US 2004-766388	20040127
US 7238720	B2	20070703		
PRIORITY APPLN. INFO.:			JP 2001-149983	A 20010518
			US 2002-147105	B3 20020515
OTHER SOURCE(S):	MARPAT 137:370094			

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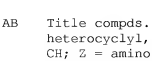

I

AB Title compds. [I; R1 = (substituted) alkyl, cycloalkyl, heteroaryl, aryl, heterocyclyl, polycycloalkyl; W = bond, alkylene, etc.; n = 0-2; X1, X2 = N, CH; Z = amino, pyrrolidinyl, thiazolidinyl], were prepared Thus, 3-(4-toluenesulfonyl)-1H-1,2,4-triazole (preparation given) was stirred with dimethylcarbamoyl chloride and K2CO3 were stirred 70 min. in DMF to give 3-(4-toluenesulfonyl)-1-dimethylcarbamoyl-1H-1,2,4-triazole. I inhibited DPPIV with IC50 = 0.000347-5.53 μM.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 20 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:849601 HCAPLUS Full-text
DOCUMENT NUMBER: 137:353024
TITLE: Preparation of 2-iminoimidazole derivatives as platelet aggregation inhibitors
INVENTOR(S): Suzuki, Shuichi; Kotake, Makoto; Miyamoto, Mitsuaki; Kawahara, Tetsuya; Kajiwara, Akiharu; Hishinuma, Ieharu; Okano, Kazuo; Miyazawa, Syuhei; Clark, Richard; Ozaki, Fumihiro; Sato, Nobuaki; Shinoda, Masanobu; Kamada, Atsushi; Tsukada, Itaru; Matsuura, Fumiyoshi; Naoe, Yoshimitsu; Terauchi, Taro; Oohashi, Yoshiaki; Ito, Osamu; Tanaka, Hiroshi; Musya, Takashi; Kogushi, Motoji; Kawada, Tsutomu; Matsuoka, Toshiyuki; Kobayashi, Hiroko; Chiba, Kenichi; Kimura, Akifumi; Ono, Naoto
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: PCT Int. Appl., 225 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002088094	A1	20021107	WO 2002-JP3952	20020419
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002251501	A1	20021111	AU 2002-251501	20020419
EP 1394152	A1	20040303	EP 2002-720536	20020419
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1503784	A	20040609	CN 2002-808565	20020419
EP 1614680	A2	20060111	EP 2005-22069	20020419
EP 1614680	A3	20060201		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
CN 1733725	A	20060215	CN 2005-10080404	20020419
CN 1754880	A	20060405	CN 2005-10080403	20020419
ZA 2003008064	A	20050207	ZA 2003-8064	20031016
US 20040242627	A1	20041202	US 2004-475045	20040611
JP 2006206595	A	20060810	JP 2006-41270	20060217
JP 2006225393	A	20060831	JP 2006-41255	20060217
PRIORITY APPLN. INFO.:			JP 2001-121829	A 20010419
			JP 2001-269422	A 20010905
			CN 2002-808565	A3 20020419
			EP 2002-724628	A3 20020419
			JP 2002-583382	A3 20020419

WO 2002-JP3952 W 20020419

OTHER SOURCE(S): MARPAT 137:353024

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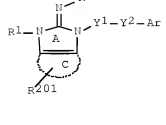

I

AB The title compds. I [ring C is a benzene ring, a pyridine ring, or the like; R1 is optionally substituted C1-6 alkyl or the like; R201 is hydrogen, halogeno, acyl, or the like; R6 is hydrogen, C1-6 alkyl, C1-6 alkyloxycarbonyl, or the like; Y1 is a single bond, CH2, or the like; Y2 is a single bond, CO, or the like; and Ar is hydrogen, Ph (generic structure given) (further details on said Ph are given)] are prepared 2-[3-(4-Aminobenzyl)-2-imino-2,3-dihydrobenzimidazol-1-yl]-1-(3,5-di-tert- butyl-4-hydroxyphenyl)ethanone dihydrochloride in vitro showed IC50 of 1.3 μM against thrombin-induced platelet aggregation.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 21 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:849599 HCAPLUS Full-text

DOCUMENT NUMBER: 137:353022

TITLE: Preparation of 2-iminoimidazole derivatives as thrombin receptor antagonists

INVENTOR(S): Suzuki, Shuichi; Kotake, Makoto; Miyamoto, Mitsuaki; Kawahara, Tetsuya; Kajiwara, Akiharu; Hishinuma, Ieharu; Okano, Kazuo; Miyazawa, Syuhei; Clark, Richard; Ozaki, Fumihiro; Sato, Nobuaki; Shinoda, Masanobu; Kamada, Atsushi; Tsukada, Itaru; Matsuura, Fumiyoshi; Naoe, Yoshimitsu; Terauchi, Taro; Oohashi, Yoshiaki; Ito, Osamu; Tanaka, Hiroshi; Musya, Takashi; Kogushi, Motoji; Kawada, Tsutomu; Matsuoka, Toshiyuki; Kobayashi, Hiroko; Chiba, Kenichi; Kimura, Akifumi; Ono, Naoto

PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan

SOURCE: PCT Int. Appl., 171 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002088092	A1	20021107	WO 2002-JP3950	20020419
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,				

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002249621	A1	20021111	AU 2002-249621	20020419
EP 1391456	A1	20040225	EP 2002-718622	20020419
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1503784	A	20040609	CN 2002-808565	20020419
EP 1614680	A2	20060111	EP 2005-22069	20020419
EP 1614680	A3	20060201		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
CN 1733725	A	20060215	CN 2005-10080404	20020419
CN 1754880	A	20060405	CN 2005-10080403	20020419
ZA 2003008064	A	20050207	ZA 2003-8064	20031016
US 20050004197	A1	20050106	US 2004-475118	20040611
US 7304083	B2	20071204		
JP 2006206595	A	20060810	JP 2006-41270	20060217
JP 2006225393	A	20060831	JP 2006-41255	20060217

PRIORITY APPLN. INFO.:

JP 2001-121829	A	20010419
JP 2001-269422	A	20010905
CN 2002-808565	A3	20020419
EP 2002-724628	A3	20020419
JP 2002-583382	A3	20020419
WO 2002-JP3950	W	20020419

OTHER SOURCE(S): MARPAT 137:353022

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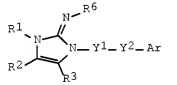

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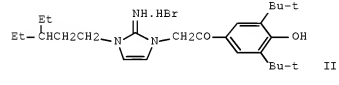

II

AB The 2-iminoimidazole derivs. represented by the formula (I) or salts thereof [wherein R1, R2, R3 = H, cyano, halo, each (un)substituted C1-6 alkyl, alkylidene, C2-6 alkenyl, C2-6 alkynyl, acyl, CO2H, CONH2, C1-6 alkoxycarbonyl, C1-6 alkylaminocarbonyl, HO, C1-6 alkoxy, etc.; or R1 and R2 are linked together to form a 5-membered ring; R6 = H, C1-6 alkyl, acyl, CONH2, HO, C1-6 alkoxy, C1-6 alkyloxycarbonyloxy, C3-8 cycloalkyl, optionally acyloxy-substituted C1-6 alkyloxycarbonyl, etc.; Y1 = a single bond, (CH2)m (wherein m = an integer of 1-3), each (un)substituted CH, CH2, NH, CONH, or SO2NH, etc.; Y2 = a single bond, O, (CH2)m (m = same as above), CO, SO, SO2, each (un)substituted CH, CH2, or C(:NOH); Ar = H, (un)substituted Ph or a 5-

to 14-membered aromatic heterocyclyl] are prepared These compds. are antagonists of thrombin receptors, in particular thrombin PAR1 receptor, platelet aggregation inhibitors, or proliferation inhibitors of smooth muscle cell, endothelial cell, fibroblast, kidney cell, osteosarcoma cell, muscle cell, cancer cell and/or glial cell. They are remedies and/or preventives of thrombosis, vascular restenosis, deep venous thrombosis, lung embolism, cerebral infarction, heart disease, disseminated intravascular coagulation syndrome, hypertension, inflammation, rheumatism, asthma, glomerulonephritis, osteoporosis, neuropathy and/or malignant tumor. Thus, a solution of 305 mg 1-(3-ethylpentyl)-1H-2-imidazoleamine and 660 mg 2-bromo-1-[3,5-di(tert-butyl)-4-hydroxyphenyl]-1-ethanone in 20 mL ethanol was heated at 60° for 3 h to give 700 mg 1-[3,5-di(tert-butyl)-4-hydroxyphenyl]-2- [3-(3-ethylpentyl)-2-imino-2,3-dihydroimidazol-1-yl]ethanone hydrobromide (II). II showed IC50 of 0.074 μM for inhibiting the [3H]Ala-(4-fluoro)Phe-Arg-(cyclohexyl)Ala-(homo)Arg-NH2 binding on human platelet membrane in a thrombin receptor binding assay, that of 0.54 μM for inhibiting the thrombin-induced human platelet aggregation, and that of 0.3 μM for inhibiting the proliferation of rat aortic smooth muscle cell.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 22 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:832759 HCAPLUS Full-text
DOCUMENT NUMBER: 137:353062
TITLE: Preparation of 2-iminopyrrolidine derivatives as thrombin receptor antagonists
INVENTOR(S): Suzuki, Shuichi; Kotake, Makoto; Miyamoto, Mitsuaki; Kawahara, Tetsuya; Kajiwara, Akiharu; Hishinuma, Ieharu; Okano, Kazuo; Miyazawa, Syuhei; Clark, Richard; Ozaki, Fumihiro; Sato, Nobuaki; Shinoda, Masanobu; Kamada, Atsushi; Tsukada, Itaru; Matsuura, Fumiyoshi; Naoe, Yoshimitsu; Terauchi, Taro; Oohashi, Yoshiaki; Ito, Osamu; Tanaka, Hiroshi; Musya, Takashi; Kogushi, Motoji; Kawada, Tsutomu; Matsuoka, Toshiyuki; Kobayashi, Hiroko; Chiba, Kenichi; Kimura, Akifumi; Ono, Naoto
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: PCT Int. Appl., 948 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085855	A1	20021031	WO 2002-JP3961	20020419
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2446924	A1	20021031	CA 2002-2446924	20020419
AU 2002255269	A1	20021105	AU 2002-255269	20020419

AU 2002255269	B2	20070315			
EP 1391451	A1	20040225	EP 2002-724628		20020419
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2002008985	A	20040309	BR 2002-8985		20020419
CN 1503784	A	20040609	CN 2002-808565		20020419
HU 2004000467	A2	20050228	HU 2004-467		20020419
EP 1614680	A2	20060111	EP 2005-22069		20020419
EP 1614680	A3	20060201			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR					
CN 1733725	A	20060215	CN 2005-10080404		20020419
RU 2270192	C2	20060220	RU 2003-133664		20020419
CN 1754880	A	20060405	CN 2005-10080403		20020419
JP 3795458	B2	20060712	JP 2002-583382		20020419
NZ 528820	A	20070126	NZ 2002-528820		20020419
NO 2003004632	A	20031219	NO 2003-4632		20031016
MX 2003PA09497	A	20040524	MX 2003-PA9497		20031016
ZA 2003008064	A	20050207	ZA 2003-8064		20031016
KR 749794	B1	20070817	KR 2003-713674		20031018
IN 2003DN01719	A	20051014	IN 2003-DN1719		20031020
US 20050004204	A1	20050106	US 2004-475188		20040609
US 7244730	B2	20070717			
AU 2005202135	A1	20050609	AU 2005-202135		20050517
AU 2005202135	B2	20071115			
KR 749795	B1	20070817	KR 2005-709505		20050526
US 20050245592	A1	20051103	US 2005-158941		20050622
JP 2006206595	A	20060810	JP 2006-41270		20060217
JP 2006225393	A	20060831	JP 2006-41255		20060217
PRIORITY APPLN. INFO.:			JP 2001-121829	A	20010419
			JP 2001-269422	A	20010905
			AU 2002-255269	A3	20020419
			CN 2002-808565	A3	20020419
			EP 2002-724628	A3	20020419
			JP 2002-583382	A3	20020419
			WO 2002-JP3961	W	20020419
			KR 2003-713674	A3	20031018
			US 2004-475188	A1	20040609

OTHER SOURCE(S): MARPAT 137:353062

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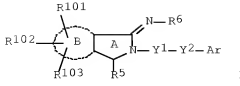

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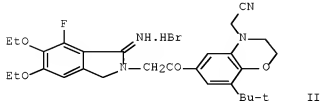

II

AB 2-Iminopyrrolidine derivs. including 2,3-dihydro-1H-isoindole and 6,7-dihydro-5H-pyrrolo[3,4-b]pyridine represented by the general formula (I) or salts thereof [wherein B = (un)substituted aromatic hydrocarbon or aromatic heterocyclic ring optionally containing 1 or 2 N atom(s); R101, R102, R103 = H, cyano, halo, each (un)substituted C1-6 alkyl, C2-8 alkenyl, C2-8 alkynyl, acyl, CO2H, CONH2, C1-6 alkoxycarbonyl, C1-6 alkylaminocarbonyl, HO, C1-6 alkoxy, C3-8 cycloalkyloxy, NH2, C1-6 alkylamino, C3-8 cycloalkylamino, acylamino, ureido, sulfonylamino, sulfonyl, SO2NH2, or C3-8 cycloalkyl, etc.; Y1 = a single bond, (CH2)m, each (un)substituted CH, CH2, NH, CONH, or SO2NH, CH2CO, SO, SO2, CO (wherein m = an integer of 1-3); Y2 = a single bond, O, N, (CH2)m, each (un)substituted CH, CH2, or C(:NOH), CO, SO, SO2; Ar = H, (un)substituted Ph] are prepared These compds. are thrombin receptor antagonists, in particular thrombin PAR1 receptor antagonists and are useful as blood platelet aggregation inhibitors and proliferation inhibitors of smooth muscle cell, endothelial cell, fibroblast, kidney cell, osteosarcoma cell, muscle cell, cancer cell, and/or glial cell and for the treatment and/or prevention of thrombosis, vascular restenosis, deep vein thrombosis, lung embolism, cerebral infarction, heart disease, disseminated intravascular coagulation syndrome, hypertension, inflammation, rheumatism, asthma, glomerulonephritis, osteoporosis, nerve disease, and/or malignant tumor. Thus, [6-[(1-imino-1,3-dihydroisoindol-2-yl)acetyl]-2,3- dihydrobenz[1,4]oxazin-4-yl]acetonitrile derivative (II) in vitro showed IC50 of 0.017 μM for inhibiting the binding of [3H]Ala-(4-fluoro)Phe-Arg- (cyclohexyl)Ala-homoArg-Tyr-NH2 to thrombin receptor of human blood platelet, that of 0.29 μM for inhibiting the human blood platelet aggregation induced by thrombin, and that of 0.0061 μM for inhibiting the proliferation of rat smooth cell.

REFERENCE COUNT: 100 THERE ARE 100 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 23 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:832755 HCAPLUS Full-text

DOCUMENT NUMBER: 137:337774

TITLE: Preparation of cyclic amidine derivatives as thrombin receptor antagonists

INVENTOR(S): Suzuki, Shuichi; Kotake, Makoto; Miyamoto, Mitsuaki; Kawahara, Tetsuya; Kajiwara, Akiharu; Hishinuma, Ieharu; Okano, Kazuo; Miyazawa, Syuhei; Clark, Richard; Ozaki, Fumihiro; Sato, Nobuaki; Shinoda, Masanobu; Kamada, Atsushi; Tsukada, Itaru; Matsuura,

Fumiyoshi; Naoe, Yoshimitsu; Terauchi, Taro; Oohashi, Yoshiaki; Ito, Osamu; Tanaka, Hiroshi; Musya, Takashi; Kogushi, Motoji; Kawada, Tsutomu; Matsuoka, Toshiyuki; Kobayashi, Hiroko; Chiba, Kenichi; Kimura, Akifumi; Ono, Naoto

PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: PCT Int. Appl., 231 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085850	A1	20021031	WO 2002-JP3949	20020419
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002251500	A1	20021105	AU 2002-251500	20020419
EP 1386912	A1	20040204	EP 2002-720534	20020419
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1503784	A	20040609	CN 2002-808565	20020419
EP 1614680	A2	20060111	EP 2005-22069	20020419
EP 1614680	A3	20060201		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
CN 1733725	A	20060215	CN 2005-10080404	20020419
CN 1754880	A	20060405	CN 2005-10080403	20020419
ZA 2003008064	A	20050207	ZA 2003-8064	20031016
US 20040254376	A1	20041216	US 2004-475060	20040611
JP 2006206595	A	20060810	JP 2006-41270	20060217
JP 2006225393	A	20060831	JP 2006-41255	20060217

PRIORITY APPLN. INFO.:
JP 2001-121829 A 20010419
JP 2001-269422 A 20010905
CN 2002-808565 A3 20020419
EP 2002-724628 A3 20020419
JP 2002-583382 A3 20020419
WO 2002-JP3949 W 20020419

OTHER SOURCE(S): MARPAT 137:337774

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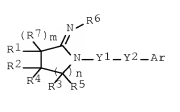

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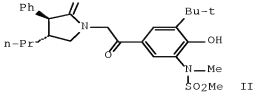


II

AB Cyclic amidine derivs. such as 2-iminopyrrolidine andhexahydrocyclopenta[c]pyrrole derivs. represented by the formula (I) or salts thereof [wherein R1-R5, R7 = H, cyano, halo, C1-6 alkyl, alkylidene, C2-6 alkenyl, C2-6 alkynyl, acyl, CO2H, CONH2, C1-6 alkoxycarbonyl, C1-6 alkylaminocarbonyl, HO, C1-6 alkoxy, C3-8 cycloalkoxy, NH2, C1-6 alkylamino, C3-8 cycloalkylamino, acylamino, sulfonylamino, sulfonyl, sulfamoyl, C3-8 cycloalkyl, 5 to 14-membered aromatic or nonarom. heterocyclyl, C6-14 aromatic cyclic hydrocarbyl; m = 0,1; or R2 and R4 are linked to each other to form a 5 or 6-membered ring containing 1-5 atoms selected from C, N, and O; or R4 and R5 together form a single bond; R6 = H, C1-6 alkyl, acyl, CONH2, HO, C1-6 alkoxy, C1-6 alkoxycarbonyloxy, C3-8 cycloalkyl, optionally acyloxy-substituted C1-6 alkoxycarbonyl, (un)substituted C6-14 aromatic cyclic hydrocarbyl or 5 to 14-membered aromatic heterocyclyl; n = 1,2; Y1 = (CH2)z (wherein z = an integer of 1-3), CH2CO, SO, SO2, CO, each (un)substituted CH, CH2, NH, CONH, or SO2NH; Y2 = a single bond, O, N, (CH2)z, SO, SO, SO2, each (un)substituted CH, CH2, or C(:NOH); Ar = H, (un)substituted Ph or 5 to 14-membered aromatic heterocyclyl] are prepared These compds. are antagonists of thrombin receptor, in particular thrombin PAR1 receptor and are useful as platelet aggregation inhibitors and proliferation inhibitors of smooth muscle cell, endothelial cell, fibroblast, kidney cell, osteosarcoma cell, muscle cell, cancer cell and/or glial cell and for the treatment and/or prevention of thrombosis, vascular restenosis, deep venous thrombosis, lung embolism, cerebral infarction, heart disease, disseminated intravascular blood coagulation syndrome, hypertension, inflammation, rheumatism, asthma, glomerulonephritis, osteoporosis, nerve disease and/or malignant tumor. Thus, to a solution of 800 mg (3S*,4R*)-2-imino-3-phenyl-4-propylpyrrolidine hydrochloride (preparation given) and 0.52 mL 1,8-diazabicyclo[5.4.0]undec-7-ene in 10 mL MeCN was added 1.32 g 3-tert-butyl-4-hydroxy-5-methanesulfonylaminophenacyl bromide and heated at 60° with stirring for 9 h to give the 2-imino-4-propylpyrrolidine derivative (II). II in vitro showed IC50 of 0.66 μM for inhibiting the [3H]Ala-(4- fluoro)Phe-Arg-(cyclohexyl)Ala-(homo)Arg-Tyr-NH2 binding on human platelet membrane, that of 2.3 μM for inhibiting the thrombin-induced aggregation of human blood platelet, and that of 2.5 μM for inhibiting the proliferation of rat aortic smooth muscle cell.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 24 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:829756 HCAPLUS Full-text
DOCUMENT NUMBER: 138:362456
TITLE: Enhanced secretion of glucagon-like peptide 1 by biguanide compounds
AUTHOR(S): Yasuda, Nobuyuki; Inoue, Takashi; Nagakura, Tadashi; Yamazaki, Kazuto; Kira, Kazunobu; Saeki, Takao; Tanaka, Isao
CORPORATE SOURCE: Tsukuba Research Laboratories, Eisai Company Limited, 5-1-3, Tokodai, Tsukuba, Ibaraki, 300-2635, Japan
SOURCE: Biochemical and Biophysical Research Communications (2002), 298(5), 779-784
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Metformin was reported to increase blood plasma active glucagon-like peptide-1 (GLP-1) in humans. There are 2 possible mechanisms for this effect: (1)

metformin inhibits dipeptidyl peptidase IV (DPPIV), an enzyme degrading GLP-1, and (2) metformin enhances GLP-1 secretion. To elucidate the mechanism(s), the authors examined (1) IC50 of metformin for DPPIV inhibition, (2) plasma active GLP-1 changes after oral biguanide (metformin, phenformin, and buformin) treatment in fasting DPPIV-deficient F344/DuCrj rats, and (3) plasma intact GLP-1 excursions after oral administration of metformin and/or Val-pyrrolidide, a DPPIV inhibitor, in fasting DPPIV-pos. F344/Jcl rats. The authors' in vitro assay showed that metformin at ≤ 30 mM has no inhibitory activity towards porcine or rat DPPIV. Metformin treatment (30, 100, and 300 mg/kg) increased plasma active GLP-1 levels dose-dependently in DPPIV-deficient F344/DuCrj rats (.apprx.1.6-fold at 3 and 5 h after administration of 300 mg/kg). This treatment had no effect on blood glucose levels. Similarly, phenformin and buformin (30 and 100 mg/kg) elevated plasma intact GLP-1 levels in F344/DuCrj rats. In DPPIV-pos. F344/Jcl rats, coadministration of metformin (300 mg/kg) and Val-pyrrolidide (30 mg/kg) resulted in elevation of plasma active GLP-1, but neither metformin nor Val-pyrrolidide treatment alone had any effect. These findings suggest that metformin has no direct inhibitory effect on DPPIV activity and that metformin and the other biguanides enhance GLP-1 secretion, without altering glucose metabolism Combination therapy with metformin and a DPPIV inhibitor should be useful for the treatment of diabetes.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 25 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:793586 HCAPLUS Full-text

DOCUMENT NUMBER: 137:310909

TITLE: Preparation of aminomethylphenylalkanoic acid derivatives as remedies for diabetes, digestive tract diseases, etc.

INVENTOR(S): Matsuura, Fumiyoshi; Emori, Eita; Shinoda, Masanobu; Clark, Richard; Kasai, Shunji; Yoshitomi, Hideki; Yamazaki, Kazuto; Inoue, Takashi; Miyashita, Sadakazu; Hihara, Taro

PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan

SOURCE: PCT Int. Appl., 100 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

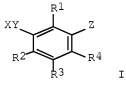
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002081428	A1	20021017	WO 2002-JP3002	20020327
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002241296	A1	20021021	AU 2002-241296	20020327
EP 1375472	A1	20040102	EP 2002-707187	20020327
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

US 20040138271	A1	20040715	US 2003-471254		20030910
US 7244861	B2	20070717			
PRIORITY APPLN. INFO.:			JP 2001-100678	A	20010330
			WO 2002-JP3002	W	20020327
OTHER SOURCE(S):	MARPAT 137:310909				

GI



I

AB The title compds. I [X represents optionally substituted aryl or heteroaryl; Y represents a group represented by the general formula CONR11CR22R33 (wherein R11, R22, and R33 each represents hydrogen, etc.), etc.; Z represents a group represented by the general formula CR111R222(CR333R444)m (wherein m is 0 to 2 and R111, R222, R333, and R444 each represents hydrogen, etc.); and R1, R2, R3, and R4 each represents hydrogen, etc.] are prepared The in vitro bioactivity of compds. of this invention vs. PPAR α, PPAR β, and PPAR γ was demonstrated.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 26 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER:	2002:793403 HCAPLUS Full-text
DOCUMENT NUMBER:	137:310931
TITLE:	Preparation of phenylalkanoic acid derivatives as preventive or remedial agents for digestive tract diseases
INVENTOR(S):	Horizoe, Tatsuo; Shinoda, Masanobu; Emori, Eita; Matsuura, Fumiyoshi; Kaneko, Toshihiko; Ohi, Norihito; Kasai, Shunji; Yoshitomi, Hideki; Yamazaki, Kazuto; Miyashita, Sadakazu; Hihara, Taro; Seiki, Takashi; Clark, Richard; Harada, Hitoshi
PATENT ASSIGNEE(S):	Eisai Co., Ltd., Japan
SOURCE:	PCT Int. Appl., 344 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	Japanese
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002080899	A1	20021017	WO 2002-JP3006	20020327

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,

CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2002242989 A1 20021021 AU 2002-242989 20020327
PRIORITY APPLN. INFO.: JP 2001-101465 A 20010330
JP 2001-105131 A 20010403
WO 2002-JP3006 W 20020327
OTHER SOURCE(S): MARPAT 137:310931
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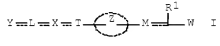

AB Disclosed is a preventive/remedy for digestive tract or inflammatory diseases, which contains as the active ingredient a novel carboxylic acid derivative represented by the following formula [I; R1 = H, OH, each (un)substituted C1-6 alkyl, C1-6 alkoxy, C1-6 alkylthio, C1-6 hydroxyalkyl, C1-6 hydroxyalkoxy, C1-6 hydroxyalkylthio, C1-6 aminoalkyl, C1-6 aminoalkoxy, C1-6 aminoalkylthio, C2-12 alkoxyalkyl, C3-7 cycloalkyl, C3-7 cycloalkyloxy, C3-7 cycloalkylthio, C2-6 alkenyl, C2-6 alkenyloxy, or C2-6 alkenylthio, etc.; L = a single or double bond, each (un)substituted C1-6 alkylene, C2-6 alkenylene, or C2-6 alkynylene; M = a single bond, each (un)substituted C1-6 alkylene, C2-6 alkenylene, or C2-6 alkynylene; T = a single bond, each (un)substituted C1-3 alkylene, C2-3 alkenylene, or C2-3 alkynylene; W = 2,4-dioxothiazolidin-5-yl, 2,4-dioxothiazolidin-5- ylidene, carboxy, (un)substituted CONH2; X = O, (un)substituted C2-6 alkenylene, hydroxymethylene, CO, CS, N-(un)substituted CQNH, NHCQ, SO2NH, NHSO2, or NHCQNH (Q = O, S); Y = (un)substituted C5-12 aromatic hydrocarbyl or C3-7 aliphatic hydrocarbyl optionally containing ≥1 heteroatoms; ring Z = C5-6 aromatic hydrocarbyl; Y = (un)substituted aromatic hydrocarbon group optionally containing ≥1 heteroatoms; some provisos given], a salt of the derivative, or a hydrate of either. The above digestive tract diseases include (1) inflammatory digestive tract diseases such as ulcerous colitis, Crohn's disease, pancreatitis, and gastritis, (2) digestive tract proliferative diseases such as digestive tract benign rumors, digestive tract polyp, hereditary (genetic) polyposis syndromes, colon cancer, rectum cancer, and stomach cancer, and (3) digestive tract ulcerous diseases such as duodenal ulcer, stomach ulcer, esophagus ulcer, regurgitant esophagitis, stress ulcer or erosion, erosion caused by drugs, and Zollinger-Ellison syndromes. The above inflammatory diseases include arthritic rheumatism, multiple sclerosis, immunodeficiency, cachexia, osteoarthritis, osteoporosis, asthma, and allergy. The compds. I are triple agonists for PPAR (peroxisome proliferator-activated receptor) α, β, and γ subtype. Thus, 2-isopropoxy-3-[4-methoxy-3- [[[4-(trifluoromethyl)benzyl]amino]carbonyl]phenyl]propanoic acid in vitro showed the transcription activity for PPARα, β, and γ with EC50 of 0.08, 2.513, and 0.382 μM, resp., in CV-1 cell. (2S)-3-[3-[[(2,4-dichlorobenzoyl)amino]methyl]-4-methoxyphenyl]-2- isopropoxypropanoic acid at 1 mg/kg/day p.o. for 3 days showed a disease activity index based on diarrhea, bloody excrement, and weight loss (DAI) of 2.0±0.3 in mice suffering from colitis induced by dextran sulfate sodium salt vs. 2.8±0.2 for the control group and 2.1±0.3 for the mice treated with rosiglitazone at 30 mg/kg/day. Many compds. prepared do not possess the thiazolidine skeleton and thereby may completely avoid toxicity such as liver disorder which was noted in the past as a problem for compds. having PPARγ agonist activity.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 27 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:777901 HCAPLUS Full-text
DOCUMENT NUMBER: 137:279098
TITLE: Preparation of oxodihydropyridinylalkanoic acids and pyridinylalkanoic acids for treatment of diabetes, insulin resistance, inflammation, etc.
INVENTOR(S): Harada, Hitoshi; Shinoda, Masanobu; Clark, Richard; Matsuura, Fumiyoshi; Emori, Eita; Kasai, Shunji; Yoshitomi, Hideki; Yamazaki, Kazuto; Inoue, Takashi; Miyashita, Sadakazu; Hihara, Taro
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002079162	A1	20021010	WO 2002-JP3003	20020327
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002241297	A1	20021015	AU 2002-241297	20020327
EP 1375484	A1	20040102	EP 2002-707188	20020327
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 20040116708	A1	20040617	US 2003-469173	20030827
US 7253178	B2	20070807		
PRIORITY APPLN. INFO.:			JP 2001-91675	A 20010328
			WO 2002-JP3003	W 20020327
OTHER SOURCE(S):	MARPAT 137:279098			

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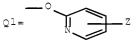


AB The title compds. Ar(CR1R2)mXCR3R4CR5R6(CR7C8)nY (I) [Ar is a group derived from a 6- to 14-membered aromatic ring which may have one or more substituents; R1, R2, R3, R4, R5, R6, R7, and R8 are each independently hydrogen, halogeno, hydroxyl, alkyl, or alkoxy; X is oxygen or methylene; Y is Q1, etc.; Z is a group represented by CR9R10CR11R12CO2H; R9, R10, R11, and R12 are each independently hydrogen, halogeno, hydroxyl, alkyl, or alkoxy; m is 0

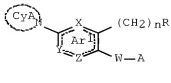
or 1; and n is 0 or 1] are prepared The PPAR agonist activity of compds. of this invention was demonstrated.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 28 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:754378 HCAPLUS Full-text
DOCUMENT NUMBER: 137:279102
TITLE: Preparation of N-aryl-substituted cyclic amine derivatives as inhibitors of squalene synthetase and medicine containing the same as active ingredient
INVENTOR(S): Okada, Toshimi; Kurusu, Nobuyuki; Tanaka, Keigo; Yoshikawa, Seiji; Shinmyo, Daisuke; Watanabe, Nobuhisa; Iruta, Hironori; Hiyoshi, Hironobu; Saeki, Takao; Yanagimachi, Mamoru; Ito, Masashi
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002076973	A1	20021003	WO 2002-JP3004	20020327
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002241298	A1	20021008	AU 2002-241298	20020327
EP 1375496	A1	20040102	EP 2002-707189	20020327
EP 1375496	B1	20070704		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
AT 366248	T	20070715	AT 2002-707189	20020327
US 20040072830	A1	20040415	US 2003-470675	20030730
US 7112593	B2	20060926		

PRIORITY APPLN. INFO.:	JP 2001-91480	A	20010327
	WO 2002-JP3004	W	20020327

OTHER SOURCE(S): MARPAT 137:279102
GI



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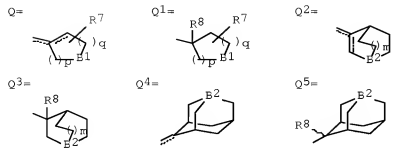

AB The title compds. [I; R1 = (un)substituted vinyl or aromatic ring ; n = an integer of 0-2; X, Y, Z = (un)substituted CH or NH, S, O; or Y = a single bond; when Y is a single bond, the ring to which X, Y, and Z belong becomes a 5-membered ring; CyA = (un)substituted 5- to 14-membered nonarom. cyclic amino or amido each optionally containing O or S; W = (un)substituted CH2CH2, CH:CH, C.tplbond.C, or phenylene, a single bond, NHCO, CONH, NHCH2, CH2NH, CH2CO, COCH2, O(CH2)m, (CH2)mO (m = an integer of 0-5), OCH2C(R2):, OCH2CHR2 (R2 = H, C1-6 alkyl, halo), NHS(O)l, S(O)lNH, CH2S(O)l, S(O)lCH2 (l = 0, 1,2); A = -C(NR3R4)R5R6, Q-Q5; R3-R6 = H, (un)substituted C1-6 alkyl, or R3 and R4 or R5 and R6 are bonded to each other through a carbon chain optionally containing a hetero atom to form a ring; R7 = H, (un)substituted C1-6 alkyl, HO, alkoxy, halo, (un)substituted NH2; R8 = H, HO, alkoxy, halo, (un)substituted NH2; B1 = (un)substituted CH or NH, O, S; B2 = (un)substituted CH or NH; p, q = an integer of 0-4 and p+q = an integer of 0-4; m = 0,1; a proviso is given], salts thereof, or hydrates of both are prepared These compds. have excellent inhibitory activity against squalene synthetase and inhibit the biosynthesis of cholesterol or triglyceride. They are useful for the prevention and/or treatment of hyperlipidemia, arteriosclerosis, ischemic heart diseases, hypertension, coronary artery disease, cerebral vascular diseases, aortic disease, peripheral vascular diseases, angina pectoris, acute coronary syndrome, or myocardial infarction. Thus, 2-benzyl-3-iodo-6-[(3R,4R)-3-hydroxy-4-methoxypyrrolidin-1-yl]pyridine was coupled with 1-tert-butoxycarbonyl-3-ethynyl-3-piperidinol in the presence of (Ph3P)4Pd, CuI, and Et3N in MeOH/DMF under reflux for 3 h to give 3-[2-benzyl-6-[(3R,4R)-3-hydroxy-4-methoxypyrrolidin-1-yl]-3- pyridyl]ethynyl-3-piperidinol (II). II and 1-[2-benzyl-6-[(3R,4R)-3- hydroxy-4-methoxypyrrolidin-1-yl]-3-pyridyl]ethynylcyclohexylamine showed IC50 of 1.4 and 0.53 μM, resp., against squalene synthetase of rat liver microsome.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 29 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:381011 HCAPLUS Full-text
DOCUMENT NUMBER: 137:107478
TITLE: Improvement of high fat-diet-induced insulin resistance in dipeptidyl peptidase IV-deficient Fischer rats
AUTHOR(S): Yasuda, Nobuyuki; Nagakura, Tadashi; Yamazaki,

Kazuto; Inoue, Takashi; Tanaka, Isao
CORPORATE SOURCE: Tsukuba Research Laboratories, Eisai Co., Ltd., 5-1-3, Tokodai, Tsukuba, Ibaraki, 300-2635, Japan
SOURCE: Life Sciences (2002), 71(2), 227-238
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB F344/DuCrj rats are genetically deficient in dipeptidyl peptidase IV (DPPIV). This enzyme degrades glucagon-like peptide-1 (GLP-1), which induces glucose-dependent insulin secretion. Glucose tolerance of F344/DuCrj rats is improved as a result of enhanced insulin release induced by high levels of plasma GLP-1. In this study, we fed F344/DuCrj rats and DPPIV-pos. F344/Jcl rats, aged five weeks, on a high-fat (HF) diet to examine the effect of DPPIV deficiency on food intake and insulin resistance. F344/Jcl rats gained significantly more body weight and consumed significantly more food than F344/DuCrj rats from Week 4 on either control or HF diet. Glucose excursion in the oral glucose tolerance test (OGTT) was improved in F344/DuCrj rats fed on the control or HF diet at all times examined, compared with F344/Jcl rats. Homeostasis model assessment (HOMA) insulin resistance values of F344/DuCrj and F344/Jcl rats fed on HF diet were higher than those of animals fed on control diet up to Week 6. However, HOMA insulin resistance values of F344/DuCrj rats fed on HF diet became significantly lower than those of F344/Jcl rats on HF diet during Weeks 8-10. The area under the insulin curve in the OGTT at Week 10 showed that the insulin resistance of HF-diet-fed F344/DuCrj rats was greatly ameliorated. Plasma active GLP-1 concns. of F344/DuCrj rats in the fed state were significantly higher than those of F344/Jcl rats. These observations suggest that DPPIV deficiency results in improved glucose tolerance and ameliorated insulin resistance owing to enhanced insulin release and inhibition of food intake as a result of high active GLP-1 levels.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 30 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:411263 HCAPLUS Full-text
DOCUMENT NUMBER: 135:162781
TITLE: Improved Glucose Tolerance via Enhanced Glucose-Dependent Insulin Secretion in Dipeptidyl Peptidase IV-Deficient Fischer Rats
AUTHOR(S): Nagakura, Tadashi; Yasuda, Nobuyuki; Yamazaki, Kazuto; Ikuta, Hironori; Yoshikawa, Seiji; Asano, Osamu; Tanaka, Isao
CORPORATE SOURCE: Tsukuba Research Laboratories, Eisai Company, Ltd., Tokadai, Tsukuba, Ibaraki, 300-2635, Japan
SOURCE: Biochemical and Biophysical Research Communications (2001), 284(2), 501-506
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Glucagon-like peptide-1 (GLP-1) is an incretin, which induces glucose-dependent insulin secretion. GLP-1 is rapidly degraded by dipeptidyl peptidase IV (DPPIV) after its release. The authors investigated whether DPPIV-deficient F344/DuCrj rats show improved glucose tolerance when compared with DPPIV-pos. F344/Jcl rats. Oral glucose tolerance test indicated improved glucose tolerance in F344/DuCrj rats, but blood glucose levels of the two strains were almost the same 120 min after the glucose bolus. Valine-

pyrrolidide, a DPPIV inhibitor, had no effect on the glucose tolerance of F344/DuCrj rats, but improved that of F344/Jcl rats. Enhanced insulin secretion and high plasma active GLP-1 levels were detected in an intraduodenal glucose tolerance test. Glucose tolerance is improved in DPPIV-deficient F344/DuCrj rats via enhanced insulin release mediated by high active GLP-1 levels. The authors' results suggest that DPPIV inhibition is a rational strategy to treat diabetic patients by improving glucose tolerance with low risk of hypoglycemia. (c) 2001 Academic Press.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 31 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:265369 HCAPLUS Full-text

DOCUMENT NUMBER: 134:295620

TITLE: Preparation and effect of 4-methoxyphenylpropionic acid derivatives useful in insulin resistance improvement

INVENTOR(S): Shinoda, Masanobu; Emori, Eita; Matsuura, Fumiyoshi; Kaneko, Toshihiko; Ohi, Norihito; Kasai, Shunji; Yoshitomi, Hideki; Yamazaki, Kazuto; Miyashita, Sadakazu; Hibara, Taro; Seiki, Hisashi; Clark, Richard; Harada, Hitoshi

PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan

SOURCE: PCT Int. Appl., 350 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001025181	A1	20010412	WO 2000-JP6788		20000929
W: AU, BR, CA, CN, HU, IL, JP, KR, MX, NO, NZ, RU, US, ZA					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
TW 262185	B	20060921	TW 2000-89120087		20000928
CA 2385081	A1	20010412	CA 2000-2385081		20000929
AU 2000074499	A	20010510	AU 2000-74499		20000929
AU 776267	B2	20040902			
EP 1216980	A1	20020626	EP 2000-962993		20000929
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY					
NZ 517719	A	20041029	NZ 2000-517719		20000929
US 6884821	B1	20050426	US 2002-88916		20000929
PRIORITY APPLN. INFO.:			JP 1999-282079	A	19991001
			JP 1999-369442	A	19991227
			JP 2000-38795	A	20000216
			JP 2000-104260	A	20000406
			WO 2000-JP6788	W	20000929

OTHER SOURCE(S): MARPAT 134:295620

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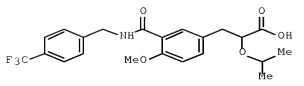

I

AB Title compds. [Y:L:X:TZM:CWR1; R1 is hydrogen, hydroxyl, alkyl; L is single bond, double bond, alkylene; M is single bond, alkylene; T is single bond, alkylene; W is carboxyl, amide; X is oxygen, alkenylene; Y is aromatic hydrocarbon; Z is aromatic hydrocarbon; colon represents single, or double bond], salts, esters, and hydrates are prepared and are useful in prevention or treatment of diabetes and X-syndrome. Thus, the title compound I was prepared and biol. tested.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 32 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:31502 HCAPLUS Full-text
DOCUMENT NUMBER: 134:100881
TITLE: Preparation of fused imidazole compounds and remedies for diabetes mellitus
INVENTOR(S): Asano, Osamu; Harada, Hitoshi; Yoshikawa, Seiji; Watanabe, Nobuhisa; Inoue, Takashi; Horizoe, Tatsuo; Yasuda, Nobuyuki; Oohashi, Kaya; Minami, Hiroe; Nagaoka, Junsaku; Murakami, Manabu; Kobayashi, Seiichi; Tanaka, Isao; Kawata, Tsutomu; Shimomura, Naoyuki; Akamatsu, Hirofumi; Ozeki, Naoki; Shimizu, Toshikazu; Hayashi, Kenji; Haga, Toyokazu; Negi, Shigeto; Naito, Toshihiko
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001002400	A1	20010111	WO 2000-JP4358	20000630
W: AU, BR, CA, CN, HU, IL, JP, KR, MX, NO, NZ, RU, US, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2376835	A1	20010111	CA 2000-2376835	20000630
AU 2000055717	A	20010122	AU 2000-55717	20000630
AU 778450	B2	20041209		
EP 1221444	A1	20020710	EP 2000-940909	20000630
EP 1221444	B1	20050831		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
NZ 516260	A	20040827	NZ 2000-516260	20000630
AT 303387	T	20050915	AT 2000-940909	20000630
PT 1221444	T	20051130	PT 2000-940909	20000630
ES 2246867	T3	20060301	ES 2000-940909	20000630
US 6841549	B1	20050111	US 2001-18688	20011220

PRIORITY APPLN. INFO.:

JP 1999-188484	A	19990702
JP 2000-143495	A	20000516
JP 2000-182786	A	20000619
WO 2000-JP4358	W	20000630

OTHER SOURCE(S): MARPAT 134:100881

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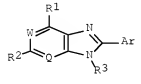

I

AB Novel fused imidazole compds. such as purine derivs. of general formula (I), pharmacol. acceptable salts thereof, or hydrates of both [wherein R1 = H, OH, halo, (un)substituted C1-8 alkyl, (un)substituted NH2; R2 = H, halo, (un)substituted NH2, (un)substituted C2-8 alkenyl, (un)substituted C3-8 alkynyl, (un)substituted C1-8 alkyl; R3 = (un)substituted C3-8 alkynyl, C3-8 alkenyl, (un)substituted C1-8 alkyl, (un)substituted aryl, (un)substituted heteroaryl, etc.; Ar = (un)substituted aryl, (un)substituted heteroaryl, optionally halo- or C1-6 alkyl-substituted N-C1-6 alkyl- or N-C3-6 cycloalkyl-oxopyridyl or -oxopyrimidyl; Q, W = N, CH; some proviso are given] are prepared These compds. exhibit adenosine A2 receptor antagonism and are effective in the prevention and treatment of diabetes mellitus and complications of diabetes. Thus, 5-[6-amino-8-(3-fluorophenyl)-9H-purin-9-yl]-1,2-dihydro-2-pyridinone was condensed with N,N-dimethylformamide di-Me acetal in DMF at room temperature for 1 h, ice-cooled, treated with NaH at 0-6° for 30 min, and methylated by Me iodide at room temperature for 16 h to give 5-[6-amino-8-(3-fluorophenyl)-9H-purin-9-yl]-1-methyl-1,2-dihydro-2-pyridinone (II). II.HCl at 10 mg/kg p.o. in spontaneously diabetic mice lowered the blood sugar level to 47.3±7.2% of the control animal.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 33 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:887079 HCAPLUS Full-text

DOCUMENT NUMBER: 134:193277

TITLE: 2-Alkynyl-8-aryl-9-methyladenines as Novel Adenosine Receptor Antagonists: Their Synthesis and Structure-Activity Relationships toward Hepatic Glucose Production Induced via Agonism of the A2B Receptor

AUTHOR(S): Harada, Hitoshi; Asano, Osamu; Hoshino, Yorihisa; Yoshikawa, Seiji; Matsukura, Masayuki; Kabasawa, Yasuhiro; Niijima, Jun; Kotake, Yoshihiko; Watanabe, Nobuhisa; Kawata, Tsutomu; Inoue, Takashi; Horizoe, Tatsuo; Yatuda, Nobuyuki; Minami, Hiroe; Nagata, Kaya; Murakami, Manabu; Nagaoka, Junsaku; Kobayashi, Seiichi; Tanaka, Isao; Abe, Shinya

CORPORATE SOURCE: Tsukuba Research Laboratories, Eisai Company Ltd, Tsukuba Ibaraki, 300-2635, Japan

SOURCE: Journal of Medicinal Chemistry (2001), 44(2), 170-179
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:193277
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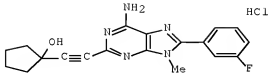

I

AB Novel adenosine antagonists, 2-alkynyl-8-aryl-9-methyladenine derivs., were synthesized as candidate hypoglycemic agents. These analogs were evaluated for inhibitory activity on N-ethylcarboxamidoadenosine (NECA)-induced glucose production in primary cultured rat hepatocytes. In general, aromatic moieties at the 8-position and alkynyl groups at the 2-position had significantly increased activity compared to unsubstituted compds. The preferred substituents at the 8-position of adenine were the 2-furyl and 3-fluorophenyl groups. In modifying the alkynyl side chain, change of the ring size, cleavage of the ring, and removal of the hydroxyl group were well tolerated. The order of the stimulatory effects of adenosine agonists on rat hepatocytes was NECA > CPA > CGS21680, which is consistent with involvement of the A2B receptor. In Chinese hamster ovary cells stably transfected with human A2B receptor cDNA, one of the compds. potent in hepatocytes, I (IC50 = 0.42 μM), antagonized NECA-induced stimulation of cAMP production (IC50 = 0.063 μM). This inhibitory effect was much more potent than those of FK453, KF17837, and L249313 which have been reported to be resp. A1, A2A, and A3 selective antagonists. These findings agree very well with the result that, compared to I, these selective antagonists for each receptor subtype showed only marginal effects in rat hepatocytes. These results suggest that adenosine agonist-induced glucose production in rat hepatocytes is mediated through the A2B receptor. Furthermore, I showed hypoglycemic activity in an animal model of noninsulin-dependent diabetes mellitus, the KK-Ay mice. It is possible that inhibition of hepatic glucose production via the A2B receptor could be at least one of the mechanisms by which I exerts its in vivo effects. Further elaboration of this group of compds. may afford novel antidiabetic agents.
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 34 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:451298 HCAPLUS Full-text
DOCUMENT NUMBER: 131:116251
TITLE: Preparation of purine derivatives as adenosine A2 receptor antagonists for the treatment of diabetes
INVENTOR(S): Asano, Osamu; Harada, Hitoshi; Hoshino, Yorihisa; Yoshikawa, Seiji; Inoue, Takashi; Horizoe, Tatsuo; Yasuda, Nobuyuki; Nagata, Kaya; Nagaoka, Junsaku; Murakami, Manabu; Kobayashi, Seiichi
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: PCT Int. Appl., 167 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9935147	A1	19990715	WO 1998-JP5870	19981224
W: AU, BR, CA, CN, HU, KR, MX, NO, NZ, RU, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
JP 11263789	A	19990928	JP 1998-363938	19981222
JP 3990061	B2	20071010		
CA 2315736	A1	19990715	CA 1998-2315736	19981224
AU 9916885	A	19990726	AU 1999-16885	19981224
EP 1054012	A1	20001122	EP 1998-961528	19981224
EP 1054012	B1	20030611		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
EP 1300147	A1	20030409	EP 2002-29118	19981224
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
AT 242775	T	20030615	AT 1998-961528	19981224
US 6579868	B1	20030617	US 2000-582840	20000705
US 39112	E1	20060530	US 2000-57854	20000705

PRIORITY APPLN. INFO.:

JP 1998-526	A	19980105
EP 1998-961528	A3	19981224
WO 1998-JP5870	W	19981224

OTHER SOURCE(S): MARPAT 131:116251
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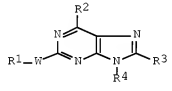

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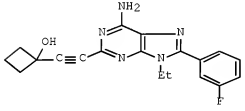

II

AB The title compds. I [R1 = (un)substituted aromatic ring (which may contain heteroatom), etc.; W = CH2CH2, etc.; R2 = H, (un)substituted alkyl, etc.; R3 = H, (un)substituted cycloalkyl, etc.; R4 = H, (un)substituted alkyl, heteroaryl, etc.; a proviso is given] are prepared In an in vitro test for A2a receptor antagonism, the title compound II showed the Ki value of 0.002 μM.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 35 OF 35 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1988:517757 HCAPLUS Full-text
DOCUMENT NUMBER: 109:117757
ORIGINAL REFERENCE NO.: 109:19493a,19496a
TITLE: Corrosion product behavior in low crud boiling water reactors
AUTHOR(S): Nagao, H.; Morikawa, Y.; Yamazaki, K.; Hemmi, Y.; Nakayama, Y.; Takagi, K.; Yoshikawa, S.; Suzuki, Y.; Otoha, K.
CORPORATE SOURCE: Toshiba Corp., Japan
SOURCE: Water Chemistry of Nuclear Reactor Systems (1986), 4(Vol. 2), 59-66
CODEN: WCNSD6; ISSN: 0950-8686
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Recent Japanese BWRs have important features concerning radiation control measures. Design bases improvements were made on reducing crud input and Co minimization. Effectiveness of these measures were qualified from operating water chemical data. Replacement of in-core materials is the most cost-effective method for Co reduction, and control of crud input from feedwater is effective for reduction of insol. 60Cu, although there is an optimum Fe concentration to maintain a low soluble Co concentration

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L4             STR L1
L5           344 SEA SUB=L3 SSS FUL L4

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                OR CLARK R/AU OR CLARK R ?/AU
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L17          28 SEA ABB=ON  PLU=ON  KIRA K/AU OR "KIRA KAZUNOBU"/AU
L18         297 SEA ABB=ON  PLU=ON  "YASUDA NOBUYUKI"/AU OR YASUDA N/AU
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                YAMAZAKI K ?/AU
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L25           9 SEA ABB=ON  PLU=ON  L16 AND (L17 OR L18 OR L19 OR L20)
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     experimental property data in the original document.  For information
     on property searching in REGISTRY, refer to:

     http://www.cas.org/support/stngen/stndoc/properties.html

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